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PART ONE · SOME PROBLEMS OF PERSONNEL RESEARCH

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Personnel Research

PERSONNEL RESEARCH is a term that has come into use in recent years to denote investigations into the physical and psychological effects of working-conditions upon efficiency, especially in relation to military operations. When we refer to men and women collectively as "personnel", we are thinking of them not as individuals, but as interdependent working units in some larger organism. It is the essence of personnel research that the healthy subject is studied in relation to his fitness to perform particular duties.

Before 1939, the Medical Research Council had undertaken a number of *ad hoc* investigations at the request of the armed forces, but the exacting demands of mechanized warfare created the need for a very considerable expansion of research into the factors influencing the efficiency of the human operator of the machines of war and the adaptation of those machines to the capabilities and limitations of those who had to use them.

This symposium is very far from constituting a comprehensive account of all the many personnel problems investigated since 1939. It does not include, for example, a discussion of important work on physiological problems of high-altitude flying—a subject which would provide enough material for a separate number of this Bulletin. The present number should not, therefore, be regarded as more than a representative selection of material.

During the recent war, the growth of personnel research took place under the direction of special committees of civilian scientists and representatives of the armed forces, and it was the Medical Research Council which provided the inspiration, the machinery, and many of the scientific staff necessary for the detailed study of the problems which came before these committees. The first of them was the Flying Personnel Research Committee, which was appointed by the Air Ministry in 1939, a few months before the war, with Sir Edward Mellanby, Secretary of the Medical Research Council, as its Chairman. In 1940, the War Office referred to the Medical Research Council some problems which led to the appointment by the Council of a Body Protection Committee, under the chairmanship of Viscount Falmouth. In 1941, the scope and membership of the committee were extended and, by agreement with the Army Council, its name was changed to the Military Personnel Research Committee. Its secretary was Dr. E. A. Carmichael, of the Medical Research Council. In 1942, the Admiralty requested the Medical Research Council to appoint a similar committee for the study of naval problems, and the Royal Naval Personnel Research Committee was accordingly established. At the Admiralty's suggestion, Sir Edward Mellanby accepted the chairmanship of this committee, which included the Medical Director-General of the Navy, the Director of Scientific Research of the Admiralty, and other representatives of the Medical Research Council, including Dr. G. L. Brown, the committee's secretary, and of the Royal Navy.

Each of these personnel research committees appointed sub-committees for the study of special problems. Among the problems studied were : the physiology of high-altitude flying; clothing of aircrews, guncrews, and others exposed to extremes of temperature or particular hazards; air- and seasickness; acoustic problems, including protection of hearing; visual adaptation, including the design of instrument-panels and the effects of glare and dazzle; the effects of drugs on performance; selection and training of personnel for general and special duties; pilot-fatigue; analysis of flying-accidents and military-traffic accidents; body-protection and steel helmets; effects of blast; crew-conditions in tank-warfare; parachute-jumping; ventilation and fume-hazards; insecticides; underwater physiology; seating of gun-crews; energy-output of crews of gun-turrets; habitability of warships.

This list indicates, in very general terms, the multiplicity of problems included as the objects of personnel research in wartime. It seems hardly necessary to labour the point that many of the methods employed are suitable for use in peacetime —not only in such obvious fields as civil aviation, but also in the more ordinary personnel problems of industry. Before the war, an organization for the study of the human unit in industry already existed in the Industrial Health Research Board of the Medical Research Council, and during the war some of the Council's staff who had undertaken studies for the Board were transferred to work for the Personnel Research Committees.

One of the consequences of the great extension of personnel research for military purposes may well be the wider application in industrial life of that open-mindedness and spirit of inquiry by which problems previously ignored or treated empirically are accepted as suitable objects of experimental study. Much of the story of personnel research has not been told, but we hope that this symposium will help to show that there are few problems, however simple they may seem, that are not illuminated by the application of the scientific method.

* * *

ACKNOWLEDGEMENTS. All but two of the papers published in this symposium are the texts of, or are based upon, communications read at two special series of meetings held by the Royal Society of Medicine on Problems of Protection and Problems of Efficiency. The papers published here include the majority, but not all, of the subjects of the communications at these meetings and, in addition, two papers by Drs. H. D. Darcus & Graham Weddell and Mr. J. S. Weiner which were contributed by special invitation. None of the papers has previously been published.

We are grateful to the Royal Society of Medicine for having allowed us to publish the papers read at its special meetings. By making use of this material, we have derived considerable benefit from the preliminary work of selection and organization undertaken by the Society.

We should also acknowledge our indebtedness to Dr. F. H. K. Green, of the Medical Research Council, for having placed at our disposal information on the organization and responsibilities of the Personnel Research Committees.

HEAT-STROKE AND HEAT-EXHAUSTION IN IRAQ

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In 1943, at the request of the British War Office, two observers were sent by the Medical Research Council to Iraq, to obtain physiological and biochemical data on cases of heat-stroke and heat-exhaustion.

Heat-Stroke

Very few cases occurred in the summer of 1943, and those that were seen conformed closely to the classical description. A man previously well would suddenly become unconscious with a rectal temperature in the neighbourhood of 110° F. [43.3° C.]. When questioned after recovery, he would usually say that he had suddenly stopped sweating; this was borne out by the fact that on examination the skin was found to be uniformly dry all over the body, including the face.

The fact that sweating stopped so suddenly and so completely suggested a breakdown in the *central* mechanism for heat-regulation. But the cause of the breakdown could not be established. Little information was derived from biochemical examination of the blood and urine. It has often been observed that frequency of micturition is a warning sign of heat-stroke; this was present in most of the cases seen in Iraq. During the first few days after admission to hospital, there was a moderate polyuria; the output of chloride in the urine was normal—a fact which seemed to rule out the possibility of salt-deficiency as an etiological factor. On the other hand, the concentrations of chloride in whole-blood and plasma were reduced; the average values were 74.1 and 88.3 milli-Equivalent per litre, compared with the control levels of 81.9 and 100.4 milli-Equivalent[1] per litre. One explanation of these findings is that the reduced chloride-concentration in the blood was a sign, not of salt-deficiency, but of haemodilution. This hydraemia, and the polyuria, might be caused by failure of sweating and the diminished fluid-loss from the skin. Thus the biochemical changes that were found appeared to be secondary, and to give no indication of the cause of the breakdown.

Experience in the Mesopotamian campaign in 1917, and again in Iraq in 1942, had suggested that heat-stroke was caused by excessive exposure or by overwork. But in the sporadic cases occurring in the summer of 1943 these factors played no part. There was no evidence of any failure in the preventive arrangements of the army. The patients had not been exposed to undue stress; if anything, they had been under less stress than usual. A number of them had just completed long journeys, coming to southern Iraq from the northern part of the country or from India. They did not become ill during the journey, but usually while resting quietly in transit camps. Because of the history of recent travelling, the cessation of sweating might be attributed to incomplete acclimatization; but this view is open to criticism, since all the cases had been in the tropics for at least several weeks, and it is known that many of the adjustments involved in acclimatization take place in the first few days of exposure to heat. In general, over-exposure to the sun, and overwork, must be regarded as factors precipitating the onset of heat-stroke, but it is clear that they are not the only cause.

Heat-Exhaustion Type 1

This name has been given to the condition referred to by some authors as " heat-shock ". Patients of this type were admitted to hospital suffering from collapse, vomiting and cramps. They showed changes of some interest in the circulatory system. The pulse-rate and systolic blood-pressure were normal when the man was lying down; the diastolic pressure was high and the pulse-pressure reduced. On standing, the pulse became very fast, the systolic pressure fell, and syncope occurred. One practical point emerged from these observations: neither the pulse-rate nor the systolic pressure, taken when the patient is lying down, give any indication of the existence or severity of this type of heat-exhaustion. The diastolic pressure is a much better guide, a high diastolic pressure being a bad sign.

In a small number of these cases the plasma-volume was measured, and was found to be greatly reduced—by 30 % to 50 %. This finding explains the cardio-vascular changes. In the effort to preserve a normal blood-pressure in the face of a reduced blood-volume, there was intense generalized vaso-constriction, manifesting itself by a rise in diastolic pressure. Sweating was profuse, and the skin was cold and clammy, but in spite of this the body-temperature was slightly raised. This was the result of diminished peripheral circulation and the reduced rate of heat-transfer from the inside of the body to the surface.

These patients had a very low urine-volume on admission, and some even had anuria; the urine was highly concentrated, and contained little or no salt. The plasma and whole-blood chloride concentrations were grossly diminished, and the blood-urea was high, reaching levels of 150 to 200 mg. per 100 ml. Protein and haemoglobin concentrations were also above control levels. These changes represent the biochemical picture of dehydration secondary to lack of salt, rather than to lack of water.

However, this state of salt-deficiency cannot be ascribed simply to an inadequate supply of salt. The average salt-issue was about 25 g. a day per man, and it is necessary to compare this with the amount of salt lost in the sweat. It was found that the chloride-concentration of the sweat was higher in the men with heat-exhaustion (average 0.44 g. NaCl/100 ml.) than in controls (average 0.27 g. NaCl/100 ml.). The former would have a negative salt-balance on an intake of 25 g. of salt a day when their daily rate of sweating reached 5.5 litres. This is not a high rate in such a climate as that of Iraq, where men could sweat at the rate of 7 litres a day when working hard. The incidence of heat-exhaustion

[1] [Milli-Equivalent = Equivalent weight $\times 10^{-3}$ in grams.—Ed.]

type 1 was closely correlated with the peaks of hottest weather. It seemed therefore that these casualties were the direct result of the heat, but that some men were predisposed, by having a high salt-concentration in their sweat, to this type of heat-exhaustion. The problem of discovering beforehand which men are likely to be affected and of instituting preventive measures is difficult, because it is not easy, under field-conditions, to collect sweat and to estimate its salt content.

Heat-Exhaustion Type 2

The second type of heat-exhaustion, called for convenience "type 2," was a condition in which symptoms predominated over signs. The symptoms consisted of dizziness, palpitation, dyspnoea, lack of sleep, and complaints of inadequate sweating. Usually the symptoms were worse in the heat of the day. At one time it seemed possible that this condition might be a particular kind of "effort-syndrome". Very often these patients said that three or four weeks before, they had had an attack of "prickly heat". As is well known, prickly heat begins as a papular rash, the papules being surmounted by tiny vesicles. As the condition clears up the vesicle bursts, leaving a little ring of scales, and later this scaling spreads. In cases of heat-exhaustion type 2, prickly heat in the healing or scaling stage was constantly present; the desquamation was particularly severe on the arms, legs and back; the face was never affected.

An attempt was made to investigate this skin-condition by objective means, in order to check the claim of inadequate sweating. It was found that the apparently dry desquamating areas of skin had a high surface-temperature (over 100° F. [37.8° C.]). Furthermore, in tests under controlled conditions, patients of this type sweated at a lower rate than normal subjects and were unable to maintain a constant body-temperature. The claim that sweating was reduced was thus confirmed, and it seems probable that the increased severity of the symptoms in the heat of the day was the result of defective sweating and the consequent rise in body-temperature.

It should be emphasized that these cases differed from those of heat-stroke in three respects: i. The onset was gradual, not sudden. ii. The failure of sweating was partial; some areas of the body, particularly the face and flexor surfaces, sweated well, while other parts were dry. iii. The changes in the skin that have been described were nearly always present, and their severity was parallel to the severity of the general condition; in cases of heat-stroke the skin was normal or showed but a mild degree of prickly heat in the acute stage. These three facts suggest that the two conditions are etiologically distinct and that the failure of sweating in heat-exhaustion type 2 was the result of *local* causes.

An attempt was made to discover what these causes were. Investigation of the pathology of the skin showed no well-marked changes. However, physicians of the Australian Army in New Guinea have described a similar syndrome in which, by means of serial sections of the skin, they found blocking of the superficial parts of the sweat-ducts and cystic dilatation of the ducts beneath the block. In the cases in Iraq, it was found that the chloride-concentration of the sweat, measured after recovery, was considerably higher than normal (0.53 g. NaCl/100 ml., compared with the control level of 0.27 g. NaCl/100 ml.). It was thought that this increase might be a phenomenon of fatigue. The higher the chloride-concentration of the sweat, the less osmotic work the glands have to do; fatigue might lead first to impairment of the power to do osmotic work, and finally to complete cessation of function. In support of this view was the fact that cases of this type occurred with increasing frequency towards the end of the summer, and not in relation to the peaks of temperature.

Another feature of this syndrome was a very marked polyuria; the men complained of frequency of micturition, and in the wards they passed enormous quantities of urine, sometimes 8 to 10 litres a day. The total chloride-output was within normal limits; there was a moderately-reduced chloride-concentration of the plasma, but no other abnormality in the blood. In these respects, except that the polyuria was more profuse, such patients resembled cases of heat-stroke.

It has not been possible to explain the connexion between the various features of this syndrome: polyuria, reduction in plasma chloride-concentration, partial failure of sweating, and a scaly lichenified condition of the skin. The australian observations suggest that a lesion of the skin is the cause of the defective sweating; the reverse however is also possible. Acute prickly heat is so common in a climate such as that of Iraq that it cannot be considered abnormal. Whenever skin which is the seat of acute prickly heat becomes dry for any reason, for instance during the cool of the night, the prickly heat begins to heal. Desquamation is characteristic of this process. If, because of fatigue of the sweat-glands, sweating began to fail, prickly heat on the dry areas of skin would begin to heal. This explanation would harmonize with the statement made by a large number of patients, that symptoms began just when their prickly heat began to disappear.

The simplest explanation of the polyuria would be that it was secondary to polydipsia, and that this occurred because the men felt dry and hot. The possibility was also considered of diminished secretion of the pituitary anti-diuretic hormone, but pituitrin in a small number of cases was found to be ineffective in curing the polyuria.

Finally, it should be emphasized that heat-exhaustion type 2, as seen in Iraq, was not a condition in which there was danger to life. No case developed into heat-stroke. But it was important from the military point of view because the incidence was high and the rate of recovery slow. It therefore involved a great wastage of manpower. With rest, normal sweating was gradually restored; none of the measures that were tried increased the rate of recovery, and no specific method was discovered either of prevention or of cure.

As a result of the field-investigation, new problems were defined, some of which in the subsequent years were investigated in greater detail in the laboratory of Dr. Ladell[2], the senior member of the Medical Research Council's team in Iraq.

[2] [See *BMB* 1013.—ED.]

* * *

EFFECTS ON MAN OF HIGH TEMPERATURES

With special reference to the work of the Heat Physiology Team at the National Hospital

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1 Problems for investigation
2 Acclimatization
3 Tolerance of raised body-temperature
4 Fatigue of sweat-glands
5 Physical limitations of evaporation
6 Some other problems studied
References

All the military services have had to contend with heat during the late war. Desert-heat with dry-bulb temperatures up to 125°F. [51·7°C.] and sun temperatures of 160°F. [71°C.] or more, and jungle-heat with temperatures of 90°F. [32·2°C.] and almost full saturation, were encountered by the Army; and the Royal Navy has had its own peculiar problems in the tropical seas in gun-turrets, where ventilation is at a minimum and temperature and humidity are both high, and in engine- and boiler-rooms where radiant heat adds to the burden (Critchley, 1945).

The heat physiology team at the National Hospital, Queen Square, London, under the direction of Dr. E. A. Carmichael, has attempted in the last four years to determine (*a*) what are the limits of tolerability of heat, (*b*) in what way the effects of heat may be mitigated, and (*c*) how, if at all, a man's tolerance to extreme heat may be increased. With the exception of one summer spent in Iraq by two members of the team, and another summer spent by another member in India, in connexion with armoured warfare, all the work has been done in "hot-rooms" in Britain, using subjects who were exposed to "tropical conditions" only during the actual experimental periods each day. Two pilot experiments have been done where the subjects remained in the hot-rooms 24 hours a day for periods up to 14 days, but no detailed results are available from these as yet.

1. Problems for Investigation

Primarily the problem of heat appeared to be a physical one. The heat produced by the body must be lost to the environment if the body-temperature is not to rise; the heat-loss is by convection, by radiation and conduction, and by evaporation. When the air-temperature is above the skin-temperature, heat is gained and not lost by convection, and if surrounding objects are also at that temperature, conduction and radiation are also adding to the heat-load of the body; in these circumstances, all the heat-loss must be by evaporation. When the air-temperature is not much below the skin-temperature, as is often the case in the tropics, convective loss is relatively small and so, again, evaporative cooling is most important. It is possible to calculate the amount of sweat that must be usefully evaporated to dissipate the metabolic heat, and this calculation has been useful in estimating the ventilation needed in tanks. In general, however, the physics of evaporation from the human body and the physiology of sweating have proved too complex for fixed rules to be formulated from theory alone, without experiment.

In an environment where most of the heat-loss must be by evaporation, the body-temperature usually rises; whether or not this rise is halted early depends upon :—

i. The capacity of the body to produce enough sweat to be evaporated in sufficient quantity for cooling.
ii. The capacity of the atmosphere to evaporate the necessary amount of water quickly enough.

The rate of evaporation is a function of humidity and of air-movement; but at temperatures above the skin-temperature the greater the air-movement the greater the convective heat-gain, and so the greater the total amount of

FIG. 1. GENERAL VIEW OF HOT-ROOM THROUGH OBSERVATION-WINDOW

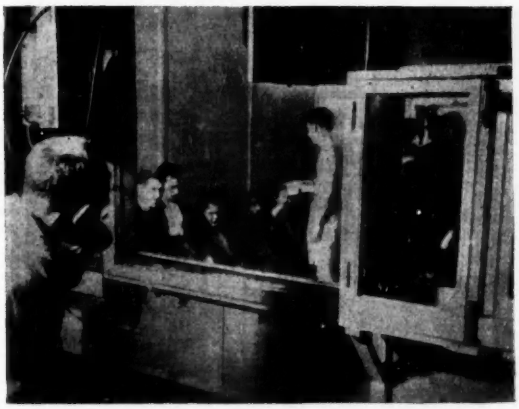
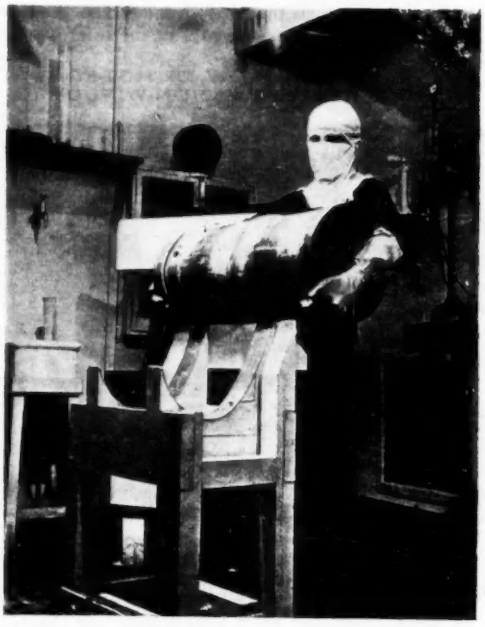


FIG. 2. HOT-ROOM, SHOWING RADIATION-PANELS AND GLOBE-THERMOMETER

FIG. 3. HOT-ROOM TEAM WITH OBSERVER

Two of the team are in antiflash clothing and the other two in shorts

FIG. 4. WORK IN THE HOT-ROOM



The subject is wearing antiflash clothing and carrying a dummy cordite-charge weighing 168 pounds [76.2 kg.]

heat to be lost by evaporation. As a first generalization, the physical factor of rate of evaporation is the limiting one in many cases, as the healthy man, after a slight initial rise in rectal temperature, usually produces more than enough sweat to cover his evaporative needs, and except in hot dry environments and with considerable air-movements there is always some unevaporated sweat; this may serve a physical function in maintaining the maximum evaporating surface. But although very high rates of sweating are needed and, in fact, found in extreme conditions (rates of 60 cm.^{3} per minute have been recorded), such rates cannot be maintained by the sweat-glands for more than about 30 minutes (Ladell, 1945a); nor are these rates achieved without preliminary training, *i.e.* acclimatization in the heat, and they are found only when the rectal temperature is considerably raised, in some cases up to 103° or 104°F. [39·4°C. or 40°C.]. Hence, though physical factors determine the limit in certain cases, physiological factors must be considered when extremes of temperature and humidity are to be endured.

The problems before us were:

Acclimatization. Of what value is preliminary hot-room training in increasing a man's ability to withstand heat; and what are the mechanisms involved in acclimatization?

Tolerance of raised body-temperature. The high rates of sweating required in extreme environments can be obtained only when the body-temperature is raised. How do men react to continued raised body-temperature?

Fatigue of sweat-glands. How long will a man continue to sweat at a steady high rate?

What are the physical limitations, in the shape of humidity and air-movement, to adequate evaporation?

2. Acclimatization

This has been studied in detail by the team, in particular by Dr. B. McArdle. Briefly, the first time a man goes into the heat he sweats poorly, his rectal temperature rises and he is not able to do much work. With successive exposures to heat and with working in the heat, his rectal temperature does not go so high, he sweats more, and his capacity to work in the heat is increased. Sweating starts at a lower rectal temperature, and later reaches a higher rate for a given rectal temperature. At the same time his cardiovascular system becomes adjusted, probably because of the increase in the plasma-volume which occurs after exposure to heat (Bazett, Sunderman, Doupe & Scott, 1940) and which we found to develop within a few hours of the first exposure.

3. Tolerance of Raised Body-Temperature

This has not been studied separately. In the course of the work, however, we have found considerable variation in tolerance; in general, the unacclimatized man appears to be more tolerant of a high rectal temperature than is the acclimatized subject, but this is largely because the acclimatized man gets a high temperature only after working far harder than can the unacclimatized man. Men are apparently physically efficient and able to continue for periods up to two hours with rectal temperatures of 102°F. [38·9°C.]. But, for other reasons, and as a result of continued observation and personal experience, a limit of 101°F. [38·3°C.] has been taken as an acceptable upper limit; if, under a given condition of clothing, work and environment, a man's rectal temperature goes above this level and remains above it for more than two hours, we consider that that set of conditions should be regarded as intolerable.

The psychological and psychomotor reactions to a raised body-temperature, and of being in the heat were studied to a small extent by Drs. J. Weiner & J. C. D. Hutchinson (1945) at the National Hospital, and more elaborate work in this field was done by Dr. N. H. Mackworth (1946) in Professor F. C. Bartlett's laboratory at Cambridge.

4. Fatigue of Sweat-Glands

The sweat-glands appear to fatigue readily at high rates of secretion (Ladell, 1945b). Sweat-rates of more than 20–25 cm.^{3} per minute are not maintained for long periods. The higher the maximum rate of sweating attained, the quicker does the rate fall away even though the environmental conditions remain the same. This is not, however, of great practical importance because :

i. In practice, conditions under which high rates of sweating are required never continue for long; *e.g.* in a gun action at sea the maximum rate of fire is seldom if ever maintained for more than 30 minutes.

ii. In hot wet environments, where the high sweat-rates are encountered, there is always more sweat produced than is required for evaporation, and so a decline in sweat-production does not have any effect on the cooling until a considerable reduction has occurred.

The decline of sweat-rate after a certain length of time takes place whether the subject is replacing his water (and salt) losses or not. The effect of water-intake and of dehydration on the rate of sweating is not marked (Ladell & Weiner, paper in preparation).

5. Physical Limitations of Evaporation

It might be expected that the physical limitations to evaporation could be simply determined by finding experimentally the limiting conditions of air-movement and humidity beyond which cooling was inadequate and the body-temperature rose. In practice it was not usually possible to do this, as intolerability is not always indicated by a steadily rising body-temperature. Subjects often failed before this point was reached; the cause was usually a failure in the circulation. Limiting environments cannot therefore be estimated from purely theoretical consideration of heat-exchange, as has been attempted by some.

The failure in the circulation in heat was studied by two members of the team, Drs. Weiner and Hutchinson, on the tilting-table. They found that pooling of blood in the legs was no greater in the heat than in the cold; nevertheless fainting occurred much sooner in the heat.

Actual limiting environments differ according as to whether the subjects are working or resting, and according to their rate of work. With an increased heat-production due to work there is a change in the heat-storage indicated by the higher rectal temperature and there is an increase in the sweat-rate. Clothing also affects the heat-loss; the effect both on temperature and on sweating is more marked in working than in resting individuals, and is least marked with high wind-velocities under hot dry conditions.

A series of experiments in which the only variable has been air-movement showed that absence of air-movement is far more deleterious than we had expected from certain published work. The effect of low air-movement is particularly noticeable at high humidities, especially when the dry-bulb temperature is high.

The points taken into consideration in deciding whether a given environment should be regarded as intolerable or not have been, for our purposes :

i. Whether one or more subjects in the group fail to stay the course of four hours.

ii. A final rectal temperature, *i.e.* after work, above 101°F. [38·3°C.].

iii. An average sweat-rate over the whole period of more than 1,250 cm.^{3} per hour.

iv. A final (after work) pulse-rate of more than 140 per minute.

By applying these criteria to our results we have been able to draw contour-lines showing the limiting environments for different conditions of work and clothing (Heat Research Team, 1944-45). Such contour-charts bring out certain points of interest. Thus, for men working in shorts :

An increase in air-movement from 10 to 25 feet[1] per minute raises the wet-bulb tolerance by 1°F. at high humidities, and by 2°F. at low humidities.

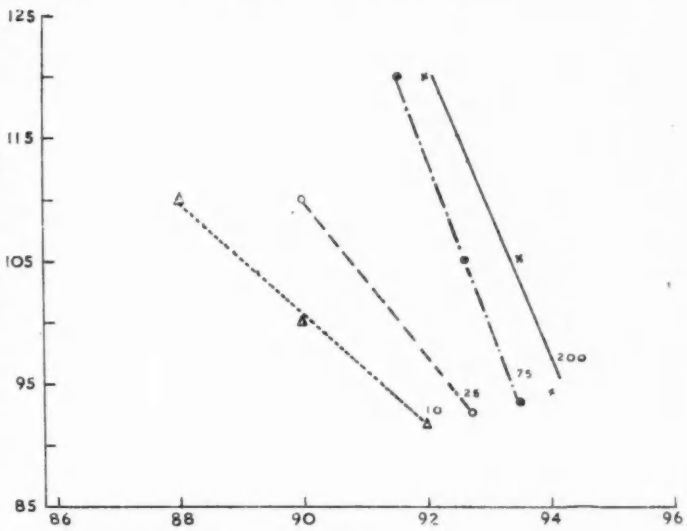
The same increase in air-movement increases the dry-bulb tolerance by 10°F. at low humidities and by 5°F. at high humidities.

An increase in air-movement from 75 to 200 feet per minute increases the wet-bulb tolerance by only 1°F. and the dry-bulb tolerance by 10°F. at all humidities.

By combining the various contour-lines and adding certain other results it is possible to construct a nomogram, from which the physiological effect of any given environment and set of conditions may be predicted.

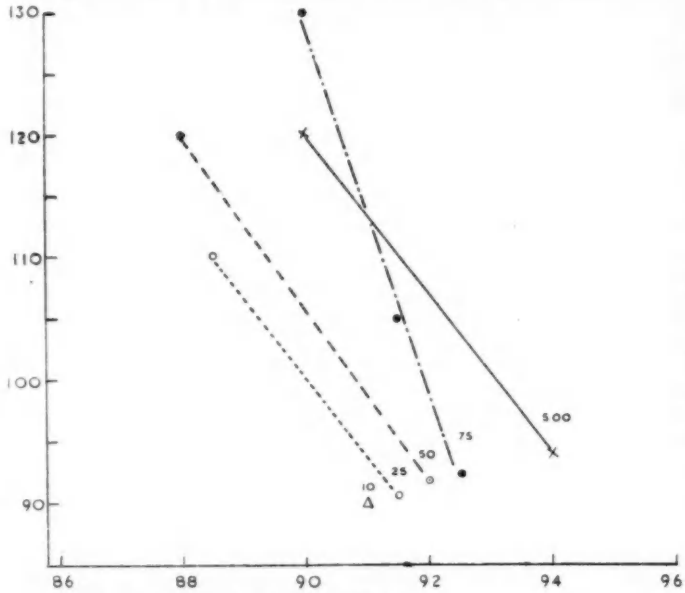
[1] [1 foot = 30·5 cm. —ED.]

FIG. 5. CONTOUR-LINES OF LIMITING ENVIRONMENTS FOR MEN IN SHORTS WORKING AT 170 kg.cal. PER HOUR



Abscissae : wet-bulb temperatures (°F.)
Ordinates : dry-bulb temperatures (°F.)
△- - - - -△ air-movement 10 feet per minute
○ — — — ○ air-movement 25 feet per minute
●—·—·—● air-movement 75 feet per minute
×————× air-movement 200 feet per minute
[1 foot =30·5 cm.]

FIG. 6. CONTOUR-LINES OF LIMITING ENVIRONMENTS FOR MEN IN SHORTS WORKING AT 196 kg.cal. PER HOUR



6. Some Other Problems Studied

In addition to the main and latest work of the team on limiting environments, there was also other work of importance in tropical warfare; these will be considered very briefly.

Armoured Warfare.

In tanks, conditions can be much worse inside than outside, owing to the heat from the engines and the moisture from the crew's breath and sweat. Dr. McArdle (1944) has designed and tested a ventilated belt which brings outside air straight under the clothes of the men in the tank and allows them to carry on under conditions which would otherwise be physiologically intolerable.

Tropical Clothing.[2]

A large number of different fabrics was tested to determine their effects upon heat-loss from the body. It was found that a thin, closely-woven, and hence mosquito-proof, fabric did not interfere with heat-loss any more than a loosely woven aertex-type fabric. In general, the thicker the fabric the more it impeded heat-loss (Ladell, 1944).

Immersion Suits

Dr. Hutchinson (1944) showed that an impermeable immersion suit when worn in air at temperatures above 90°F. [32·2°C.] was physiologically intolerable; hence one-man-submarine operators, for example, were advised not to don their suits until as late as possible, and should doff them as soon as surfacing. Similar work was done by Hutchinson on other types of diving-suits to determine how long the suit could safely be worn on the deck by a man waiting to dive. Once in the water, even in swim-suits, Hutchinson found that the body-temperature fell in sea temperatures as high as 80°F. [26·7°C.].

Anti-G-Suits[3]

In hot environments, the influence of each extra layer of clothing on the heat-loss is very marked. Experiment showed that it was almost essential to incorporate the Anti-G-suit in the ordinary flying-suit in the tropics (Hutchinson, 1944).

General Equipment

Many different items of equipment and certain weapons were tried out in the hot-rooms to determine their effect on the heat-balance of men wearing or carrying them. Other items were tested on their own account to determine the effect of heat upon them and, hence, their durability under tropical conditions.

ACKNOWLEDGEMENTS. I wish to thank my colleagues of the Heat Research Team for permission to quote from their results, and for their help in preparing this paper; and especially to Dr. McArdle for the loan of charts and for valuable criticism.

[2] [See also *BMB* 1016.—ED.]

[3] [Suits designed to protect the pilot of an aircraft from the vascular effects of acceleration.—ED.]

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EFFECTS ON MAN OF RESTRICTED WATER-SUPPLY

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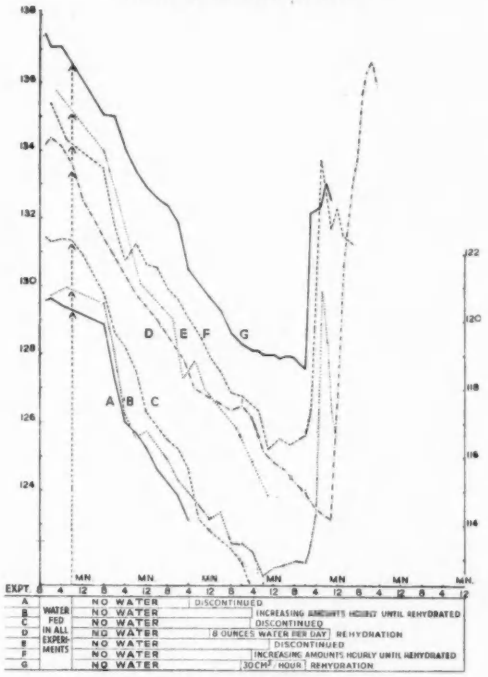
1 Physiology of water-lack
2 Lifeboat-rations
3 Possible measures for increasing water-supply in lifeboats
4 Water-rations in the tropics
References

The Committee for the Care of Shipwrecked Personnel initiated work on water-rationing in lifeboats in late 1941. The experimental work was done by Dr. J. C. D. Hutchinson at Cambridge and by myself at the National Hospital, Queen Square, London; in addition one experiment was carried out by Dr. Kenneth Mellanby, using conscientious objectors as subjects. The objects of all the experiments were to discover means of mitigating thirst, to determine the minimum water-requirements of the body, and to see how these requirements could be reduced. The experiments necessitated, therefore, that the subjects should be without water, or have only very small quantities of water, for periods up to twelve days, and at the same time, to make conditions more comparable with actual survivals, that they should eat only the prescribed lifeboat-ration which has a water-content of not more than 2%.

1. Physiology of Water-Lack

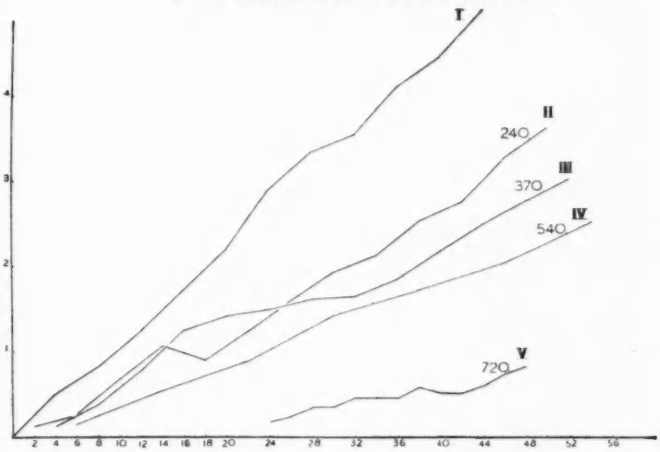
The preliminary experiments showed that there is a rapid fall in body-weight when little or no water is being taken (fig. 1). This is due to the cumulative water-debt which is contracted within the body as water is lost in the breath, through the skin, and in the urine. By gradually increasing the water-intake until the weight-loss was halted, it was found that a water-intake of between 800 and 900 cm.³ per day was needed to maintain water-balance in a temperate climate (fig. 2). When the water-intake is insufficient to prevent water-debt, the rate of urine-secretion falls off, until after about 24 hours it reaches a minimal, basal, level below which it never falls, even when there is complete deprivation of water. This basal level of urine-secretion varies according to the diet; on a carbohydrate diet it may be below 300 cm.³ per day, but on a protein diet it is as much as 500 cm.³ per day. While the volume of urine is falling, the blood-urea is rising; we found that after 24 hours without water the blood-urea was between 50 and 60 mg. per 100 cm.³ and it remained at this level until drinking was started (fig. 3).

FIG. 1. BODY-WEIGHT CURVES DURING WATER-DEPRIVATION


D E F G
A B C
MN
EXPT.
A NO WATER DISCONTINUED
B WATER FED NO WATER INCREASING AMOUNTS HOURLY UNTIL REHYDRATED
C NO WATER DISCONTINUED
D IN ALL EXPERIMENTS NO WATER 8 OUNCES WATER PER DAY REHYDRATION
E NO WATER DISCONTINUED
F NO WATER INCREASING AMOUNTS HOURLY UNTIL REHYDRATED
G NO WATER 30 CM³ / HOUR REHYDRATION

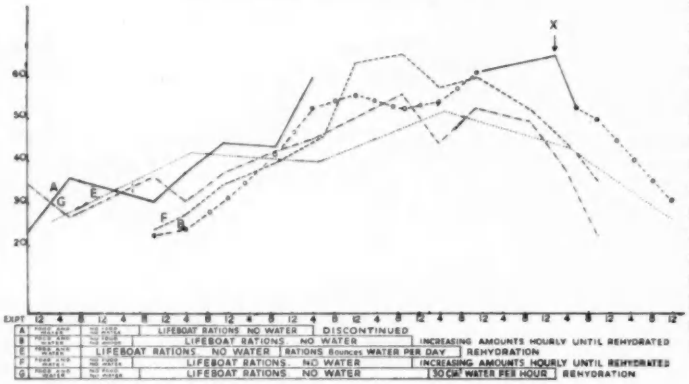
Abscissae : time in hours (MN. = midnight)
Ordinates : Right side : weight in pounds, subject RJR (A, B, C)
Left side : weight in pounds, subject WSSL (D, E, F, G)
[1 pound = 0·454 kg.]

FIG. 2. RATE OF WEIGHT-LOSS WITH DIFFERENT WATER-INTAKES



Abscissae : time in hours
Ordinates : % weight-loss
I : 2 subjects (WSSL & RJR), 5 experiments ; day 2, 3
II : 1 subject (WSSL), 1 experiment ; day 3, 4
III : 2 subjects (WSSL & THG), 1 experiment ; day 2, 3
IV : 15 subjects (Royal Naval Hospital, Haslar) ; day 2, 3
V : 1 subject (WSSL), 1 experiment ; day 4
Arabic numerals on the graph show water-intakes in cm.³ per day

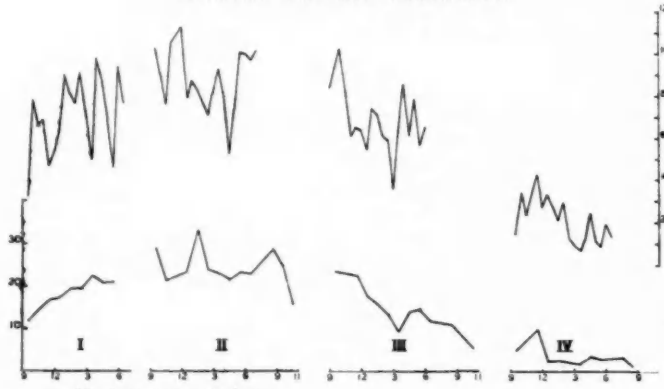
FIG. 3. BLOOD-UREA CHANGES DURING WATER-DEPRIVATION



Abscissae : time in hours
Ordinates : mg./100 cm.³
A, B, E, F, G : subjects of experiments (for explanation, see fig. 1)
X : sample unsatisfactory

From further experiments, and detailed examination of the early experiments, we showed that the physical deterioration ran parallel with the weight-loss. A 5% loss in body-weight, obtained after 24 hours' abstention, was tolerable; but with a 10% loss, such as occurred after 60 hours' deprivation, gross deterioration, physical and mental, began to set in. There was a general weakness rather than a specific failure of one or more systems; even after 3 days' total deprivation, a subject could still rally himself to perform an exercise-tolerance test efficiently, and though on walking there might be a foot-drop, neurological examination showed no muscular weakness or changes in the reflexes.

FIG. 4. CHANGES IN SALIVARY ACTIVITY DURING WATER-DEPRIVATION



Abscissae : time in hours
Ordinates : Right side (upper) : wetness (mg. increase in weight of standard piece of lint in standard position within mouth, in 2 minutes)
Left side (lower) : volume of saliva in cm.³ collected by sucker in 15 minutes
I : water fed
II : first waterless day
III : second waterless day
IV : third waterless day

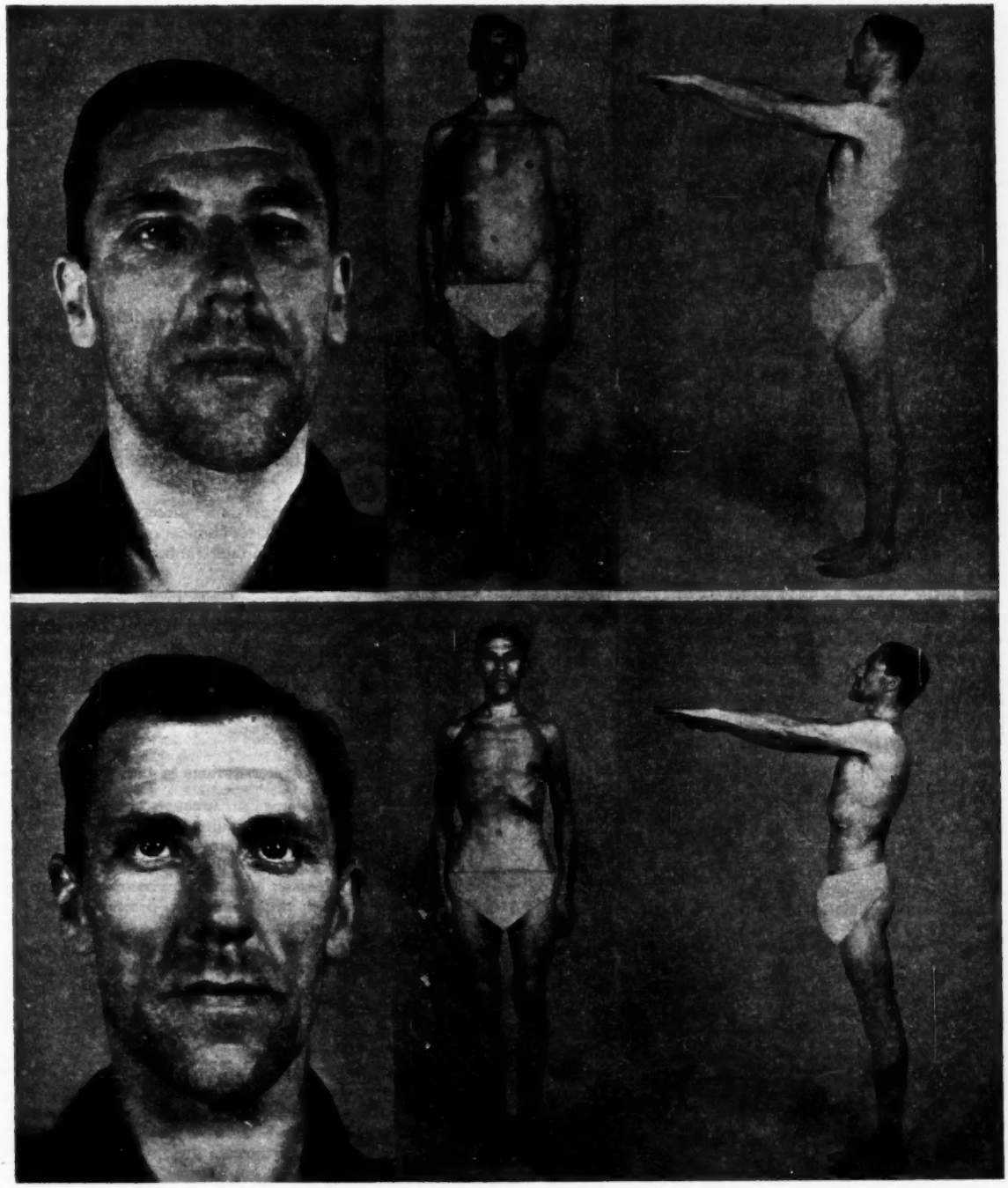
The rate of weight-loss during the first 24 hours without water is greater than the subsequent rate of loss. Urinary secretion is still at a high level, and there are no obvious signs of water-lack. Thus, the rate of salivation does not decline until there have been nearly 36 hours without water (fig. 4). Moreover, water given during the first 24 hours never saved body-water, but swelled the urine-volume by the amount taken. We concluded, therefore, that there is in the body what could be called free circulating water, normally used for such things as the intestinal secretions, which are only temporarily lost to the body during digestion and are then reabsorbed. Until this water has been utilized it is un-economical to start taking the limited water-ration. We therefore recommended that for the first 24 hours adrift no water should be taken.

2. Lifeboat-Rations

In the course of these experiments it was found that certain of the constituents of the Ministry of War Transport Ration had a diuretic effect on men even when in severe water-debt. Thus the urinary excretion of one subject was doubled, over a three-hour period, after taking 1 ounce [28 g.] of pemmican ; there was a compensatory reduction in urinary secretion later. This effect was traced to the nitrogenous extractives present in the pemmican and also to the protein in it. The urea resulting from the metabolism of protein has itself a diuretic effect. Fats and carbohydrates do not increase the urinary output. An alteration in the lifeboat-ration was therefore proposed. The old ration consisted of one ounce each per day of pemmican, of malted-milk tablets (both containing protein), of biscuits and of chocolate. The calorific value of this was 400 Cal., and the basal urine-volume on such a diet was 500 cm.³ per day. The proposed new ration consisted of one ounce each of dehydrated butter-fat or margarine, special high-fat-content biscuits, chocolate, and sweetened condensed milk (this is relatively low in protein). This ration provides 500 Cal. per day, and the basal urine-volume was found to be below 400 cm.³ per day, a considerable saving.

A lifeboat carries 112 ounces [3·18 l.] of water per person. It was customary to ration this at the rate of 8 ounces [230 cm.³] per day for 14 days. But with a water-intake of only 8 ounces daily, we found experimentally rapid deterioration; and in actual practice there had been cases where survivors had succumbed to water-lack while on this ration, lifeboats being found with people dying of thirst while there was still water in the breakers. Some other rationing plan was therefore necessary to make the best possible use of the limited water available for keeping survivors in good condition as long as possible. We had found that, although not in water-balance, men with an intake of 500–600 cm.³ of water per day remained in moderately good condition (see fig. 5); we therefore devised and recommended the following plan. (Medical Research Council, 1943.)

FIG. 5. EFFECTS OF RESTRICTED WATER-SUPPLY



Upper photographs show subject immediately before restriction of water-rations
Lower photographs show subject on the tenth day of the regime recommended in the text (immediately before the experiment was terminated)
This subject had a sea-water supplement of 180 cm.³ per day on days 2-6 inclusive

Day 1— no water.
Days 2–6— 18 ounces (512 cm.³) per day.
Thereafter—the remaining 22 ounces [625 cm.³] to be given in token quantities only, say 2 ounces per day, to maintain morale.

One large-scale experiment was carried out on volunteer naval-ratings, at the Royal Naval Hospital, Haslar, in which water-supplies were utilized in this way (Ladell, 1943). There was excellent correspondence between the observed and the predicted body-weight changes during the period of relatively high water-intake; but on the token-intake only, deterioration was not so rapid as had been expected. This suggests that there may be, in a slow dehydration, some acclimatization or habituation to water-lack. In a more rapid dehydration, however, there is not time for this to take place, and weight-loss is sometimes more rapid than expected.

3. Possible Measures for Increasing Water-Supply in Lifeboats

Various measures of increasing the water-supply were investigated:

Drinking Seawater

The kidney can excrete only up to 2% sodium chloride, whereas seawater contains 3·5%. But if the ration is almost salt-free, as it is, and as some urine is always excreted, it should be theoretically possible to drink small quantities of seawater without drawing on the body-water to excrete the salt, or accumulating salt in the body. A number of experiments was therefore carried out in which subjects drank either saline or real seawater (Ladell, 1943). In theory, the maximum permissible amount of seawater that can be drunk is 400 cm.³ per day, taken in small instalments throughout the day; in practice we found that any seawater drunk promoted a diuresis; but at intakes of less than 400 cm.³ per day, the increase in the urine-volume was less than the volume of seawater drunk; there was, therefore, a net gain of water to the body. At very low intakes, this gain amounted to about one third of the seawater drunk, but at 400 cm.³ per day the gain was less. The effect of this increased urine-volume and slight water-gain was shown by the lower blood-urea (fig. 6). When more than 400 cm.³ of sea-water is drunk daily, the urine-volume rises still more; there is an extra drain on the body-water and also some accumulation of salt within the body. Hence larger amounts of seawater are definitely dangerous (Elkinton & Winkler, 1944). Because of the difficulty of limiting to the safe level the amount of seawater to be drunk, and of the very great danger of taking too much, the Committee did not recommend the actual drinking of seawater; but it did sanction the dipping of biscuits into the sea, and rinsing the mouth with seawater. For my part, I would have no hesitation in drinking up to the prescribed amount were I ever a castaway.

Salvaging the Breath-Moisture and Body-Stills

Dr. Hutchinson and also Dr. G. L. Brown constructed several ingenious apparatuses in which the water in the breath was condensed, but the volume recovered each day was so small, about 150 cm.³, that it would have been more economical to utilise the space taken up by the apparatus to carry water. Body-stills, in which heat from the body was used to distil seawater, were made by Dr. Hutchinson, but these were also unpractical and never adopted.

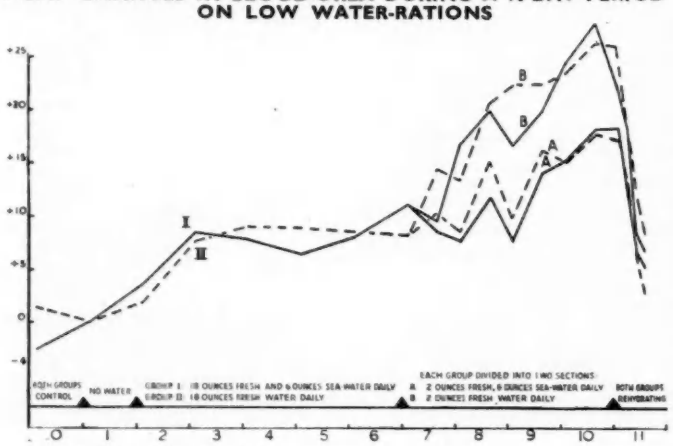
Fuel- and Sun-Stills

There has recently been some success in producing a fuel-operated still which is economical of space. The RAF have an excellent sun-still in their rubber dinghies.

Desalting Apparatus

In Dr. B. S. Platt's laboratory, and later in the laboratory of the Water-Pollution Research Board, a mixture of ionic-exchange resins which removes the acid- and the alkaline-ions together has been developed. A potable and palatable water is obtained from seawater. The final model adopted by the RAF gives 6 volumes of water for each volume occupied by apparatus and reagents.

FIG. 6. CHANGES IN BLOOD-UREA DURING A 10-DAY PERIOD ON LOW WATER-RATIONS



Abscissae : time in days
Ordinates : blood-urea increase (mg./100 cm.³)
I (unbroken line) : mean for group 1 (10 subjects)
II (broken line) : mean for group 2 (11 subjects)

4. Water-Rations in the Tropics

Water-rationing in lifeboats leads us to the question of water-rationing in the tropics. In a hot climate, water-losses are very great owing to the heavy demands of the sweat-glands. A man deprived of water in the tropics becomes dehydrated very quickly; thus one subject deteriorated more in 12 hours without water in Iraq, with the air-temperature 100°–105°F. [37·8°C.–40·6°C.], than he had done in 4 days of deprivation in England. In such rapid dehydration there are definite signs of circulatory failure, which are not apparent in the slower dehydrations carried out in England. Direct observation in Southern Iraq showed that healthy men might regularly be sweating 10 litres per day; a survey carried out before the height of the summer showed that men were drinking, on an average, nearly 7 litres of water or other fluids per day. Nevertheless, they were all producing less than 1,000 cm.³ urine daily. During the very hot weather many men lost weight, the rate of urine-secretion fell to near the basal level seen in water-debt, and the blood-urea rose. We

Continued at foot of page 13

EFFECTS OF A TROPICAL CLIMATE ON MEN IN WARSHIPS

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1 Effective temperature scales
2 Thermal environment of the men
3 Health of the men
4 Effect on efficiency
5 Conclusion
References

It is generally acknowledged that the efficiency of a ship's company depends largely upon the conditions in which it lives and works. The efficiency of the ship as a fighting unit however depends on attaining a reasonable balance between the requirements of material and those of personnel, and this is rarely a simple problem. The amount of equipment and the numbers of men who can be safely fitted into any ship fall within certain closely defined limits if the addition of excessive topweight, which may alter the stability of a ship and possibly cause it to capsize, is to be avoided.

During the early years of the recent war, a satisfactory balance between material and personnel was difficult to achieve. Vast increases of offensive and defensive equipment and additional men to operate the new weapons had to be accommodated in warships, to prosecute the war against the enemy in submarines and in the air, as well as in surface craft. Close-range weapons and high-angle guns were greatly increased in numbers. Aircraft-carriers carried more aircraft, aircrews and maintenance staff, than were ever envisaged by their designers or builders. The loss of certain ships, partly because of slow flooding along the mess-deck flats and ventilation trunking, caused emphasis to be placed on the control of flooding by turning the ship into a series of watertight sections and compartments. The valves controlling the fresh-air supply to many parts of ships were closed whenever action was imminent. All these factors detracted from the standard of living and working conditions which could be maintained, especially in warm climates, but at that time the effort was primarily concentrated on material considerations rather than on those of the personnel. Ships were being produced by the building yards at a maximum rate to fight the Battle of the Atlantic, and the first requirement was to clothe and equip the ships' companies for arctic warfare.

After the surrender of the Italian Fleet in 1943, and the immobilization of the majority of effective German Units

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EFFECTS ON MAN OF RESTRICTED WATER-SUPPLY

Continued from page 12

concluded from this that the weight-loss was due to dehydration, and we put forward the doctrine that every man should drink sufficient to produce "at least a beer-bottle and a half" [about 850 cm.³] of urine each day. Thirst is a very poor indicator of water-need; in conditions where the water-turnover is high, a man left to drink according to his fancy rarely drinks sufficient and he becomes voluntarily dehydrated; this has been shown particularly by Adolph (1943) in America.

Where there is sweating, salt-intake is as important as water-intake. In Southern Iraq, water-supply was adequate and the men were trained to drink enough, yet there were many cases of dehydration; we found this to be a salt-deficiency dehydration. At high steady rates of sweating a large amount of salt may be lost each day and this must be replaced. In the hot-room we have found sweat containing up to 0·6 % of sodium chloride; but in the field we rarely got a sample from a healthy man containing more than 0·33 %, and the average for all our samples was 0·29 %. This discrepancy between "field-sweat" and "hot-room sweat" is well known. We have been able (Ladell, 1945) to show its cause:—

i. In the hot-room, the rate of sweating is usually very much greater than in the field, as conditions are more severe and the subject is made to work harder. The greater the rate of sweating, the higher the chloride content of the sweat.
ii. Sweat-glands are susceptible to fatigue. A sweat-gland when fatigued excretes sweat with a higher concentration of chloride than when fresh. Thus, the longer a man sweats the greater the chloride content of his sweat. This fatigue-phenomenon is more marked in subjects who go into the heat only for a few hours each day than in subjects who live in the heat, either in a tropical country or in the hot-room. If a man lives in the heat, his sweat-glands become less susceptible to fatigue, and the increase in chloride-content with lengthening duration of sweating is not found. This is a type of acclimatization.
iii. We have shown that the greater the salt intake the greater the chloride-concentration in the sweat. In the field, men are not so salt-conscious as in the hot-room, and they probably take less salt.

The actual salt-requirement is simply calculated by taking 0·35 % as a safe upper level for the chloride-content of the sweat. If a man is going to sweat 10 litres per day he will lose about 35 g. of sodium chloride daily. This must be replaced, and he should also have a little in reserve, say 5 g., for any sudden extra work; it will usually not be needed and will be found in the urine. The total intake aimed at therefore must be 40 g. per day; 15 g. will always be provided by the food, without any flavouring, the rest should be taken as cruet, as salt tablets, and in the drinking water.

ACKNOWLEDGEMENTS. I wish to thank Dr. E. A. Carmichael for his help and encouragement during many of the experiments described in this article, and I am indebted to Dr. B. S. Platt for his concept of water-debt.

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in northern Europe, the imminence of an extended campaign at sea against the Japanese raised once more the question of whether the british ships, which had operated effectively in temperate and northern waters, would be able to adapt themselves satisfactorily to the tropics, where the seawater, at temperatures ranging from 80 to 90°F. [26·7 to 32·2°C.], would act as a warm water bath for the ships, instead of exercising the cooling effect it does in home waters; the moisture content of the air would be 2-3 times as great; and the ships' superstructures would be exposed throughout the day to the tropical sun.

In order to provide the Naval Staff with a reliable measure of the effect of the changed climatic conditions on efficiency, the Medical Research Council was asked by the Admiralty in May, 1944, to define the upper desirable limits of environmental warmth, for working and living compartments in ships, which were compatible with reasonable efficiency and health; and secondly, to estimate the loss of efficiency and health which would accrue if these limits were exceeded. A Sub-Committee of the Royal Naval Personnel Research Committee was set up to deal with these problems, and, at a later date, this Sub-Committee was asked to consider more general problems of warship habitability.

A preliminary recommendation based on the knowledge available at that time was made to the Admiralty, employing the American Effective Temperature Scale which appeared to be the most suitable measure of warmth available.

1. Effective Temperature Scales

The Effective Temperature Scale, first constructed by the late Commander Houghten of the United States Navy, & Yagloglu in 1923, expresses in one figure the combined effects of air-temperature, humidity, and air-movement upon the comfort-sensations of individuals. The scale is referred to standard conditions of still and saturated air. The normal effective temperature of an environment within a compartment therefore indicates that temperature of still air saturated with water-vapour in which an equivalent sensation of warmth, to that experienced by those in the compartment, would be reported by the average man or woman. The other reactions of the body to warmth have been found to correspond closely to the warmth sensations in relation to this scale. The recommendation made, which was largely based on the advice of T. Bedford and B. McArdle of the scientific staff of the Medical Research Council, and of Surgeon Captain MacDonald Critchley and Surgeon Lieutenant-Commander H. E. Holling, who had carried out a survey of living and working conditions in the Mediterranean and Far East in 1943, was that an effective temperature of 80°F. [26·7°C.] constituted the upper desirable limit for working and living compartments, and that 86°F. [30°C.] effective temperature was the upper acceptable limit above which inefficiency would have to be accepted.

The effective temperature implies that the temperature of the walls and contents will be of the same order as the air-temperature of a compartment. When the mean radiant temperature of the surroundings is significantly greater than the air-temperature, as it may be in engine-rooms, it is important to make an allowance for the factor of radiant heat. To achieve this, globe-thermometer readings are substituted for the dry-bulb readings in the determination of the effective temperature, and the resultant figure is termed the corrected effective temperature (Bedford, 1946). The upper desirable and acceptable limits of corrected effective temperature were again 80 [26·7°C.] and 86°F. [30°C.] respectively.

The cooling effect of air-movement on men stripped to the waist is very much greater than it is on men who are lightly but completely covered. Another scale of warmth, the Basic Effective Temperature Scale, constructed from observations made on men stripped to the waist, may be used for describing mess-deck conditions in the tropics where men are scantily dressed, and once more, the upper desirable basic effective temperature is 80°F. [26·7°C.] and the upper acceptable limit 86°F. [30°C.]. In this discussion, however, reference will be made only to the normal effective temperature scale, as men are always clothed in overalls at action stations, even in the tropics, as a measure of protection against flash burns.

It was now necessary to test the validity of this scale by psychological and physiological methods, and to determine the various combinations of thermal conditions at which men were likely to become partially or wholly inefficient in the performance of mental and physical work. Two series of experiments to this end were commenced at the Psychological Laboratory, Cambridge, and at the Medical Research Council Research Unit at the National Hospital in London. In these experiments, naval ratings were studied as they carried out mental and physical tasks, similar to those required of them aboard ship, in specially constructed chambers where the atmospheric thermal conditions were carefully controlled. The third line of attack was to make accurate measurements of the thermal environment, according to the effective temperature-scale in the working and living spaces of all classes of H.M. Ships in the Eastern Fleet which was then gathering at Trincomalee, and to observe any ill-effects of heat on the health or efficiency of the ships' companies.

2. Thermal Environment of the Men

It is to this third aspect of the problem that I would like to refer in greater detail, and to mention a few of the results which were obtained during a broad survey which was carried out towards the end of 1944 in 11 representative warships of the Eastern Fleet. In the assessment of the thermal conditions, the air-temperature and humidity were determined with the sling hygrometer, the degree of air-movement with a silvered katathermometer (cooling range 130–125°F. [54·4–51·7°C.]), and radiant heat, from hot machinery or sunbaked bulkheads, was expressed either in terms of the mean radiant temperature (calculated from the readings of the globe-thermometer, the dry-bulb temperature of the air, and the air velocity), or in terms of the corrected effective temperature.

The average thermal environment in these ships, based on a fairly large number of measurements, is seen to be ranged around the upper critical level at which it was thought that inefficiency due to excessive warmth might occur (table I). The average effective temperature in the living-spaces was 84°F. [28·9°C.], but in working-spaces, such as the engine-rooms, 88·7°F. [31·5°C.], in radar offices 86·9°F. [30·5°C.], and in the critical gun-control positions (high-angle calculating positions and transmitting stations) 86·5°F. [30·3°C.]. In certain compartments effective temperatures of the order of 91, 92 and 93°F. [32·8, 33·3 and 33·9°C.], were recorded, which constitute unacceptable conditions by any standards.

TABLE I. AVERAGE THERMAL ENVIRONMENT IN ELEVEN SHIPS OF THE EASTERN FLEET (1944)

	Compartment Conditions						Outside Conditions		
	Normal effective temperature (°F.)[1]	Dry-bulb temperature (°F.)[1]	Wet-bulb temperature (°F.)[1]	Air-movement (feet per minute)[2]	Absolute humidity (grains[3] per pound[4] of dry air)	Number of observations	Dry-bulb temperature (°F.)[1]	Wet-bulb temperature (°F.)[1]	Absolute humidity (grains[3] per pound[4] of dry air)
Mess-decks	84·0	90·0	82·0	100	151	947	83·1	76·6	128
Machinery-spaces	88·7	102·7	87·7	468	176	359	84·0	77·6	134
Gunnery-control positions	86·5	95·5	84·2	172	160	364	84·8	77·7	133
Gun-turret lower quarters	86·6	91·9	84·9	60	171	125	82·2	76·7	132
Radar offices	86·9	97·7	83·8	160	152	59	84·3	77·8	134
Electrical spaces	89·5	104·7	82·6	147	161	81	83·5	76·7	128
Workshops	87·5	100·3	83·7	193	149	55	83·7	76·7	128
Sickbays	83·0	90·9	82·1	239	155	82	84·1	78·1	138
Communication offices	85·8	95·9	83·9	163	156	168	84·4	77·6	132
Galleys	87·4	97·5	84·2	192	155	168	82·9	76·1	125

[1] [To convert F.° to C.°, subtract 32 and multiply by 5/9 —ED.]
[2] [1 foot = 30.5 cm.—ED.]
[3] [1 grain = 0.06 gram—ED.]
[4] [1 pound = 0.45 kilogram—ED.]

There is insufficient space to discuss in detail the many problems arising from heat-radiation in machinery compartments, workshops, galleys and sometimes in radar offices, the greatly increased significance of the wet-bulb temperature in the tropics, or the importance of adequate air-movement in ensuring comfort. The mean radiant temperature of the surroundings was at times as much as 70°F. [21·1°C.] in excess of the air-temperature, and, in 30 % of the compartments where radiation was measured, lay between 120 and 150°F. [48·9 and 65·6°C.]. When ships were closed down at sea it was found that certain workshops, galleys and many positions in machinery compartments were untenable except for short periods. Corrected effective temperatures, ranging from 95 to 100°F. [35 to 37·8°C.] were not uncommon.

TABLE II. COMMON CAUSES OF ILL-HEALTH IN 28 SHIPS AND 6 NAVAL SHORE-ESTABLISHMENTS OF THE EASTERN FLEET, FEBRUARY TO OCTOBER, 1944

Rates per 100 man-months

Section of the community (man-months)	All skin diseases including boils but excluding prickly heat	Boils alone	Otitis externa	Dysentery and allied disorders	Minor injuries	Common cold
All operational ships (128,194)	9·19	2·64	1·84	2·31	3·8	1·45
Depot-ships (28,863)	10·96	2·64	3·01	4·08	5·99	2·02
Shore establishments (131,700)	5·75	0·82	0·99	1·83	2·09	1·1
All ships & shore establishments (288,757)	7·79	1·81	1·57	2·27	3·24	1·38

Total cases reporting at the sick-bay, comprising cases placed on either the sick-list or the attending-list.

3. Health of the Men

In order to examine the effect on the men of living in a hot wet environment, reports made by ships' medical officers in reply to a questionnaire on sickness were analyzed, and the results were expressed as rates per 100 man-months. Information is normally available of the numbers of men on the sick-list each quarter in each ship or establishment, but it was expected that a more important index of the health of the community would be afforded by the numbers who attended as outpatients with minor complaints.

For a five-month period during 1944 the average numbers reporting at the sick-bay every month varied between 30 (destroyers) and 40 (cruisers) per 100 men for the average ship's company. Only 3 to 6 men per 100 of these men were placed on the sick-list, and the remainder were treated as outpatients.

Skin diseases accounted for much ill-health (table II). Even when prickly heat, which was widely prevalent and affected 80 % to 90 % of men at one time or another, was excluded from consideration, it is seen that 9 out of every 100 men in operational ships reported at the sick-bay every month with skin trouble. Conditions were slightly worse in depot- and repair-ships which remained in harbour, but very much better in the shore establishments where the rate was practically halved. Boils alone caused

TABLE III. LESS-COMMON CAUSES OF ILL-HEALTH IN 28 SHIPS AND 6 NAVAL SHORE-ESTABLISHMENTS OF THE EASTERN FLEET, FEBRUARY TO OCTOBER, 1944

Rates per 100 man-months

Section of the community (man-months)	Heat exhaustion	Malaria	Common cold	Pulmonary tuberculosis	Neuro-psychiatric disease
All ships (157,057)	0·42	0·08	1·56	0·02	0·04
Shore-establishments (131,700)	0·04	0·76	1·17	0·02	0·11

Total cases reporting at the sick-bay, comprising cases placed on either the sick-list or the attending-list.

3 out of every 100 men to report sick each month. Thus, skin diseases dwarfed all other morbid conditions in importance. By no means all of the ratings affected reported sick, and so the true incidence is understated by these figures.

In comparison with the conditions shown above, malaria was relatively unimportant in the Eastern Fleet as a cause of manpower-wastage in ships (0·08) and also in shore establishments (0·76) (table III). The common cold (1·56), a diagnosis which covered a multitude of ills, probably caused more wastage than any of the fevers, if intestinal disorders are excluded. Overcrowding of the mess-decks had not increased the incidence of pulmonary tuberculosis (0·02) above the rate of 2 per 1000 per year, which has been reported by Dudley (1941) as the naval rate for 35 years before 1939, probably because ventilation-fans were operated at the maximum practical speeds, and up to 60% of the men slept on deck in camp-beds whenever they were able to do so. From these returns, neuropsychiatric illnesses (0·06) did not appear to be a serious source of trouble in ships, but, according to Cameron (1945), hospital experience at Trincomalee showed that 7% of all naval hospital admissions, a high figure, was due to psychiatric illness, and, furthermore, he considered heat to be an aggravating or causative factor in 48% of cases. The effects of extreme heat are indicated by a reported rate of 0·42 per 100 man-months for cases of heat exhaustion, or one man for every 240 men afloat each month. Again, many heat disorders falling short of true heat exhaustion were included under this heading.

Experience gained in analyzing this questionnaire led to the construction of a new monthly return from all ships reporting major and minor illnesses as recorded at midnight on Wednesday each week. I understand from Surgeon Commander Fraser Roberts, the Consultant in Medical Statistics to the Navy, that examination of the returns for the seven months, August, 1945, to February, 1946, inclusive, shows the rates for both major and minor illness in the Fleets in the East to be rather more than double those for ships in Home Waters.

The variable incidence of prickly heat in a cruiser and a battleship showed how widely the state of health varied in different ships. Inspections of ratings on the mess-decks before they turned in at about nine o'clock in the evening showed that in the battleship, out of an average number of 479 ratings who were examined when stripped to the waist, 26% had severe prickly heat of the upper body, and 33% had mild prickly heat. In the cruiser, on the other hand, only 2% of 337 ratings had mild prickly heat. The average environmental conditions on the mess-decks of these ships, which lay only a few cables[5] from each other, were of much the same order (effective temperatures 82·7 and 83·6°F. [28·2 and 28·7°C.] respectively), and it is believed that this marked difference in the incidence of prickly heat was because the cruiser spent more time at sea, had a better fresh-water supply, better mess-deck ventilation, and had recently visited temperate waters.

4. Effect on Efficiency

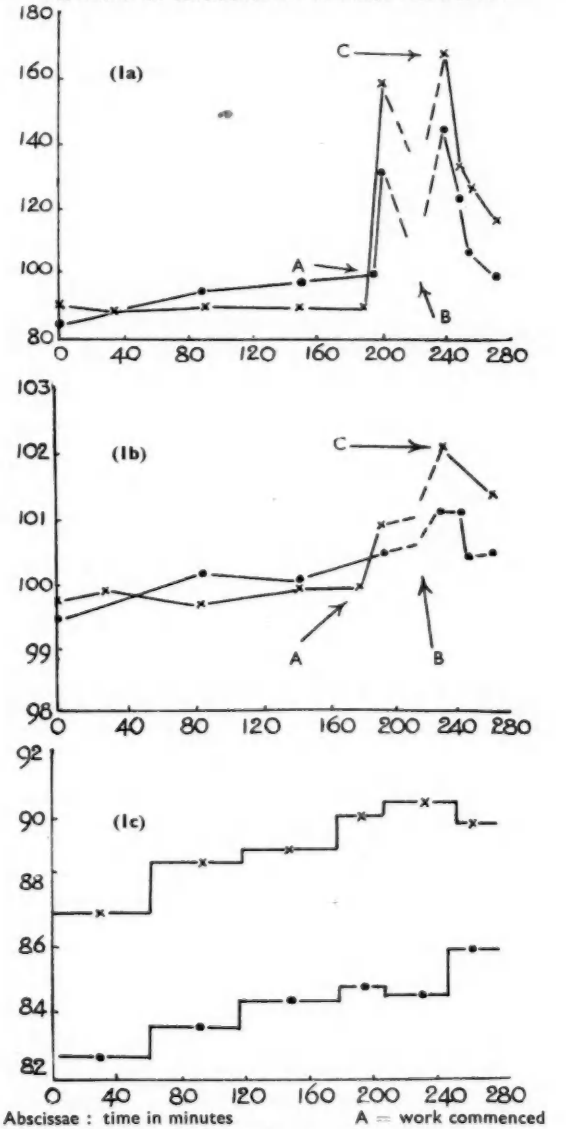
Evidence of frank breakdown of efficiency was not easy to find. Authoritative opinion stated time and again that work took longer to do, and that the quality of the work was inferior to the standards attained in the Home Fleet.

[5] [1 cable = 182.9 m.—Ed.]

There was some anxiety as to whether crews, handling heavy charges in the cordite-magazines and handing-rooms, at the bottom of the big gun-turrets in the battleships, would be able to maintain a satisfactory supply of ammunition

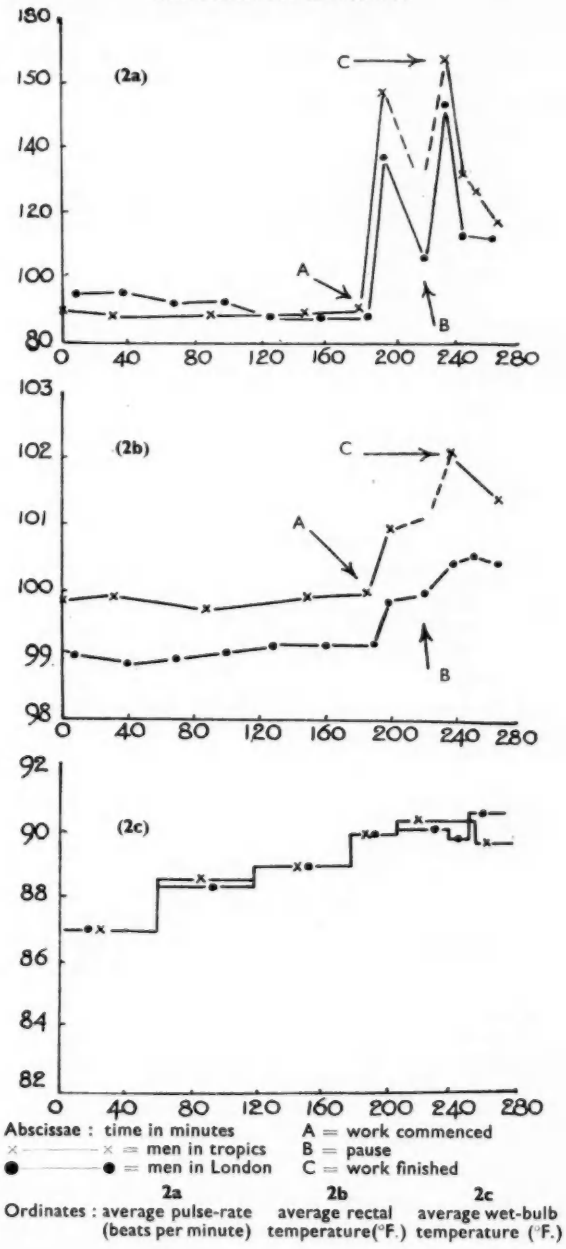
FIG. 1. AVERAGE EFFECTS OF HEAVY WORK ON CREWS OF A GUN-TURRET MAGAZINE AND A CORDITE HANDING-ROOM IN THE TROPICS

The magazine was air-conditioned. The cordite handing-room was neither air-conditioned nor ventilated with fresh air



during a prolonged action, when the fresh-air ventilation to these compartments would be closed down in accordance with precautions to be taken against the danger of flash and flooding (fig. 1).

FIG. 2. AVERAGE EFFECTS OF HEAVY WORK ON THE ACCLIMATIZED CREW OF A CORDITE HANDING-ROOM IN THE TROPICS AND ON AN ARTIFICIALLY-ACCLIMATIZED CREW DOING SIMILAR WORK UNDER THE SAME THERMAL CONDITIONS IN A CLIMATIC CHAMBER IN LONDON



In order to examine this problem the magazine and cordite handing-room crews of a large gun-turret were closed up under action conditions off Trincomalee, and after a period of three hours' resting they carried out a typical loading-exercise, simulating the effort required in a moderately severe bombardment, and comprising two equal periods of hard work separated by a rest-pause. Measurements of rectal temperature, pulse-rate, blood-pressure, body-weight and fluid balance were made on the 6 hardest-worked members of the crew in each compartment. The air-supply to the magazine was recirculated through a freon cooling-machine which also extracted moisture from the air. The air in the cordite handing-room was neither cooled, nor recirculated, so that there was little air-movement. There was no fresh-air ventilation to either compartment. During the morning the wet-bulb temperature of the magazine rose from 82 to 86°F. [27·8 to 30°C.] (average effective temperature 85°F. [29·4°C.]), but in the cordite handing-room the wet-bulb temperature rose from 87 to 90°F. [30·6 to 32·2°C.] (average effective temperature 90°F.).

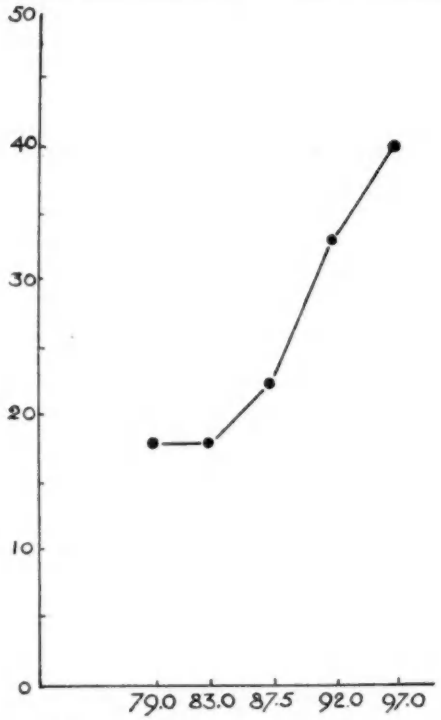
As a result of the violent exercise it is seen that the average body-temperatures (102·4°F. [39°C.]) and pulse-rates (166) of the cordite handing-room crew rose to much higher levels than those of the magazine crew (101·2°F. [38·4°C.] and 144), and several of the ratings were on the verge of collapse. There was no doubt that if the crew in the handing-room had remained closed up for many hours under the prevailing conditions they would not have have been able to maintain the supply of ammunition for a satisfactory rate of fire. Conditions in the magazine were more acceptable but were still severe for such heavy work.

In this way information was obtained on which short-term policy could be based. Ventilation routines were adjusted to give a working compromise between the requirements of damage-control and the ensuring of an environment in which men could work efficiently. Minor structural modifications and alterations to improve local conditions were instituted, and data were obtained for formulating recommendations for the future.

Similar methods were also used in the machinery-spaces, and attempts were made to measure the deterioration of mental efficiency of men manning the gunnery-control positions.

It is of interest to see how the results obtained in the Fleet were correlated with the exhaustive studies made on the naval ratings at the National Hospital, London, and at Cambridge. McArdle and his colleagues (Benson, Colver, Ladell, McArdle & Scott, 1945) at the National Hospital repeated as closely as possible the cordite handing-room trial described above (fig. 2). The thermal conditions, shown here as wet-bulb temperatures, were practically identical during the trial with the conditions recorded in tropical waters. The men had been artificially acclimatized to heavy work of this type at high temperatures by daily exposure and wore tropical-action dress. It was found that the men working in Britain tolerated both the work and the warmth with less physiological disturbance than the men who were acclimatized to the tropics, because they were well trained for heavy work at high temperatures, whereas the men in the warship, although they lived in a tropical climate, worked in the excessive warmth of the cordite handing-room only at irregular intervals, and many of them had sedentary duties at other times.

FIG. 3. EFFECT OF HOT CLIMATES ON WIRELESS-TELEGRAPHY OPERATORS HEARING AND RECORDING MORSE MESSAGES



Abscissae : effective temperature in room (°F.)	=	79	83	87.5	92	97
Corresponding dry-bulb temperatures (°F.)	=	85	90	95	100	105
Corresponding wet-bulb temperatures (°F.)	=	75	80	85	90	95

Wind-velocity = 100 feet per minute

Ordinates : percentage of faulty messages

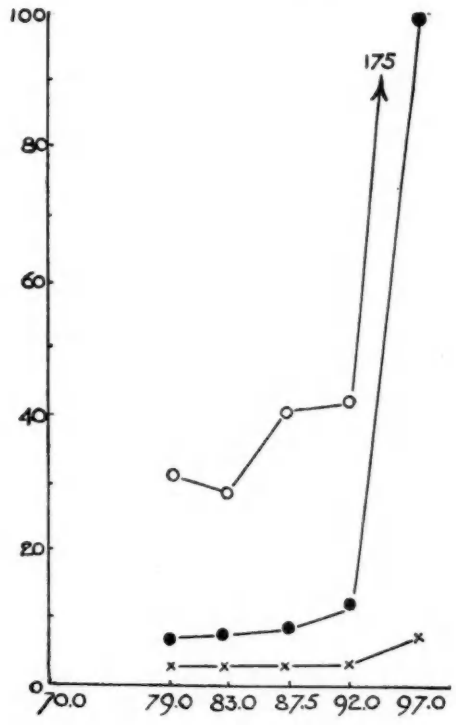
[1 foot = 30.5 cm.]

We have observed that the average effective temperatures in wireless and radar offices were approximately 86 and 87°F. [30 and 30·6°C.] respectively, and in some radar offices effective temperatures of 89 or 90°F. [31·7 or 32·2°C.] were repeatedly recorded. At Cambridge, Mackworth (1945; 1946) investigated the effect of heat on the efficiency of naval and Royal Air Force wireless-telegraphy operators working under similar conditions to those in ships (fig. 3). Efficiency was found to decline when the effective temperatures lay between 83°F. and 87·5°F. [28·3 and 30·8°C.], and declined rapidly at higher temperatures. There was considerable human variation (fig. 4), and it is seen that, whereas the competence of the average operator started to deteriorate above an effective temperature of 83°F., the very good operator could withstand extremely high temperatures and give a good performance.

Subjects carrying out the Clock Test for prolonged visual search, which simulates the psychological functions required of radar operators, and dressed only in shorts, reacted rather differently to the heat (fig. 5). The smallest number of mistakes was made at an effective temperature of 79°F. [26·1°C.], with a significant increase in the numbers of errors in the warmer climate of 87·5°F. [30·8°C.]. It was also found that these lightly-clad men made more mistakes at an effective temperature of 70°F. [21·1°C.], than similarly-clad men working at 79°F. [26·1°C.]. Adverse effects upon efficiency are thus shown to be caused by chilling as well as by warmth.

The possibility must be borne in mind that conclusions reached from studies on men working for short periods each day in hot environments in Britain may not be applicable to fully-acclimatized men in the tropics. The information gained must be verified, therefore, by confirming the more important results in the tropics, and a laboratory is to be set up for this purpose in the near future.

FIG. 4. EFFECT OF HOT CLIMATES ON WIRELESS-TELEGRAPHY OPERATORS HEARING AND RECORDING MORSE MESSAGES, SHOWING GROUP VARIATION IN PERFORMANCE



Abscissae : effective temperature in room (°F.)	=	70	79	83	87.5	92	97
Corresponding dry-bulb temperatures (°F.)	=	75	85	90	95	100	105
Corresponding wet-bulb temperatures (°F.)	=	65	75	80	85	90	95

Wind-velocity = 100 feet per minute

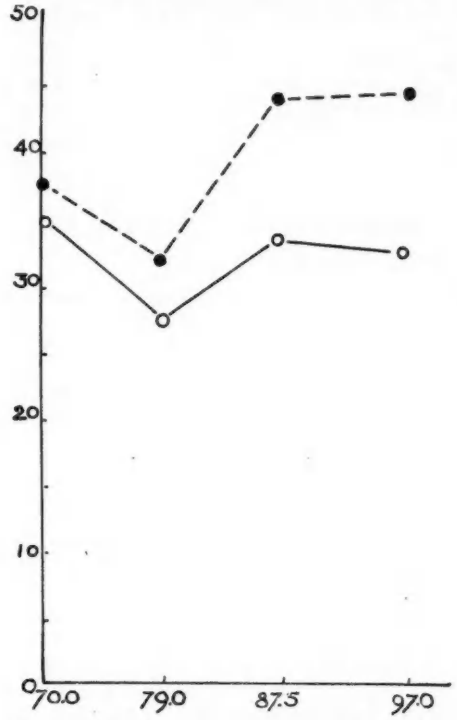
Ordinates : average number of mistakes per man per hour

○——○ = competent operators

●——● = very good operators

×——× = exceptionally-skilled operators

FIG. 5. CLOCK-TEST FOR PROLONGED VISUAL SEARCH AT DIFFERENT ROOM-TEMPERATURES, SHOWING INCIDENCE OF MISSED SIGNALS



Abscissae: effective temperature in room (°F.) = 70 79 87.5 97
Corresponding dry-bulb temperatures (°F.) = 75 85 95 105
Corresponding wet-bulb temperatures (°F.) = 65 75 85 95
Wind-velocity = 100 feet per minute
Ordinates : percentage of missed signals
○———○ = first hour of test
●- - - -● = second hour of test

5. Conclusion

We have briefly reviewed the thermal environment of the men in the Fleet in Eastern Waters under wartime conditions, the effect of climate on health, and some of the effects of heat on efficiency. The application of research in laboratories to provide answers to practical problems has been discussed. There has been no time to refer to problems of accommodation, fresh-water supplies, hygiene or catering, and to the importance of adequate general amenities and recreational facilities, but it is agreed that unless these requirements are fully implemented, efficiency will suffer and morale will deteriorate.

The visit to the Eastern Fleet had a practical as well as an academic side. A naval constructor, with an expert knowledge of ventilation and air-conditioning, was a member of the team, and he provided not only the engineering answers for improving unsatisfactory conditions, which enabled short-term improvements and modifications to be carried out, but, in addition, his technical knowledge was essential for a full appreciation of the situation. The importance of including a heating and ventilation engineer, and, if possible, a lighting expert, in any party surveying living and working conditions, whether ashore or afloat, cannot be stressed too forcibly.

The study of the effects of extremes of climate on efficiency and health are still in their early days in the Navy. The effects of excessive cold are largely unexplored. Enough information has, however, been gained in the last two years to show that the dividends paid by research more than justify the considerable efforts required.

ACKNOWLEDGEMENTS

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My thanks are also due to Dr. Brian McArdle and his colleagues, and to Dr. N. H. Mackworth and Dr. K. Cameron, who have allowed me to refer to their unpublished reports.

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BIOLOGICAL ASSESSMENT OF CLOTHING FOR TROPICAL SERVICE USE

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1 Assessment of heat-load of clothing
a Physical considerations
b Physiological test-methods
2 Mosquito-proofness
3 Physical properties of clothing and fabrics
4 Fabrics for action-rig and jungle-suits
5 Some features in design
6 Conclusion
References

During the recent war a remarkable variety of clothing-problems affecting the efficiency of military personnel was brought forward for investigation. As is well known, many specialized garments and clothing-assemblies were required for the complex and often peculiar operations which characterized, for example, the Commando and other combined operations and reconnaissance raids, midget-submarine activities, and underwater demolition, apart from the frequently-changing requirements of the regular armed forces. The present paper deals only with the physiological problems encountered in providing action-rig and other protective clothing for use in tropical climates, and is based on the research activities of the wartime Climatic Unit[1] (National Hospital, Queen Square) of the Medical Research Council.

The clothing-problems investigated by the Unit for the Army in regard to jungle-warfare, for certain shore-personnel of the Navy, for combined operations and for the Fleet Air Arm, deep diving, etc., had all in common the problem of assessing and reducing the heat-load to a degree commensurate with the desired operational requirements. In addition to the thermal properties of the clothing, a number of other factors had to be considered. The most important of these was the mosquito-proofness of fabrics, and this was regarded as a first priority in recommending fabrics suitable for use in action-rig and jungle-uniforms. A matter of interest to the Navy was that of "flash" protection; while attention had also to be given to resistance to tear and abrasion, and at different times to wetability, waterproofness and buoyancy. Apart from the particular properties of the fabric-construction, there was the question of design. This was of prime importance in the specialized protective clothing for the uses already mentioned. In some cases the design was specified by the Service concerned, and only minor modifications could be entertained; in others, as in the case of ventilated tank-suits, novel development-work was carried out.

It is not proposed in this paper to give a detailed description of these multifarious clothing-enquiries, but to use the results as far as possible for discussion of some of the more general findings, which may perhaps have a wider applicability. In particular, the methods used in assessing the thermal properties of clothing and mosquito-proofness merit some attention; while an outline of the fabric-properties and certain features of design suitable for tropical conditions may also be of some interest.

1. Assessment of Heat-Load of Clothing

a. Physical Considerations

The evaluation of the physiological role of clothing in a particular situation does not, in principle, involve any very difficult physical problems. In practice, however, and particularly when considering tropical climates, a very elaborate procedure is necessary for a complete analysis of the heat-exchange between the active clothed man and the environment. This is true even of the simpler cases where the subject is maintained in a steady condition of energy-output in a constant environment. Such studies, in which the function of the clothing as worn, in terms of its thermal properties—its thermal insulation, its resistance to moisture-diffusion, its surface-coefficients of loss of heat and water-vapour, or its effect on the "environment" at the skin-surface, have been carried out in the laboratory on small numbers of subjects and with very few types of clothing, and usually with the subject at rest (Winslow, Herrington & Gagge, 1938; Killick & Weiner, 1942, 1946; Ogden & Rees, 1946). A consideration of the thermal interchanges in such laboratory studies will indicate the main facts about the methods necessarily adopted in the studies of clothing and fabrics for military use.

In conditions approximating to "physiological" equilibrium, the change in heat-content undergone by the clothed body over a period of time may be expressed for the present purpose as the familiar heat-balance equation:

$$S = (M - W) - (E_r + E_s) \pm (C + R) \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (1)$$

where S = rate of accumulation (positive or negative) of heat in the clothed body;
M = rate of energy-output by the clothed subject;
W = rate of energy-output appearing as external work;
E_r = rate of heat-loss from the respiratory tract (most of this is evaporative heat-loss);
E_s = rate of evaporative heat-loss from the body-surface;
C = rate of heat-loss (or gain) by convection at the body-surface;
R = rate of heat-loss (or gain) by radiation at the body-surface.
$(M - W)$ expresses the heat-production term; $(E_r + E_s)$ the evaporative heat-loss and $(C + R)$ the non-evaporative or "sensible" heat-loss.

In painstaking laboratory studies, all these separate components can be measured, and it is possible to achieve a complete partition of heat-loss into its various channels through the clothing and from the clothed surface to the surroundings. This requires a large number of measurements on every subject. For example, to assess the insulation-value of the clothing, the following relations need to be determined:

[1] The MRC workers concerned in tropical clothing research were E. A. Carmichael (Director), J. C. D. Hutchinson, W. S. S. Ladell, B. McArdle and J. S. Weiner.

$$I_{Cl} = \frac{T_s - T_a}{H_s} - I_a \quad \text{..... (2)}$$

where I_{Cl} = insulation-value of the clothing;
I_a = insulation of the air at the particular wind-velocity;
T_s = average skin-temperature of the subject;
T_a = ambient air-temperature;
H_s = heat-flow through the clothing = (C + R) in formula (1)

To obtain I_{Cl} it is necessary, therefore, to determine H_s and therefore to measure the terms M, W, E and S in formula 1. The average temperature of the skin under the clothing needs also to be measured for the term in equation 2, and also, because it enters in the measurement of S, the change of heat-content of the body—a function of the change in mean temperature of the body, its mass, and its specific heat. The mean temperature (T_b) of the body is obtained from the average skin-temperature T_s measured in at least a dozen spots, and from the internal temperature T_r measured in the rectum, according to Burton's (1935) formula: $T_b = 0{\cdot}33T_s + 0{\cdot}67T_r$.

The " ventility " of the clothing to passage of moisture-vapour may be expressed as a function of the pressure-gradient of water-vapour through the clothing, and of the rate of flow of water-vapour evaporated from the skin. The measurement of the vapour-pressures under the clothing presents some problems (Ogden & Rees, 1946; Killick & Weiner, 1946), while the " ventility " measurement itself is of limited value, since in most situations of military interest, the clothing becomes wet with un-evaporated sweat, the clothes may stick to the skin-surface, and the effective evaporating surface may be that of the wet clothing. Exact measurement of evaporation from the sweating man (E_s) by means of weight-loss requires, of course, an allowance for the absorbed water in his clothing, and also for other unevaporated moisture such as runs on to the floor, into his boots, etc. The difficulty of measuring the loss by " drip " often makes the measurement of evaporative loss quite inaccurate.

It is obvious that the more precise analysis of clothing-performance indicated in the foregoing, though carried out in a modified form on a few occasions by the MRC unit, does not lend itself to the assessment of large numbers of fabrics, or to comparisons on many subjects, as is so necessary in dealing with military problems. Laboratory studies are, in any case, marred by the difficulty of simulating important features of military conditions, where states of equilibrium both of the subject and the environment, and consequently of his clothing, are probably the exception rather than the rule.

b. Physiological Test-Methods

It is therefore not surprising that, in most of the clothing-tests, the procedure has to be greatly simplified, and only indirect estimates of the thermal properties can usually be made. The usual simplifications made in regard to the terms of the heat-balance equation (equation 1 above) are as follows. The heat-output term (H − W) is standardized throughout the tests at a level and in a sequence of work- and rest-bouts not too remote from actual conditions. The MRC unit found that stepping on and off a 1-foot-high[2] stool at various rates and for bouts of 5 minutes or more provided a satisfactory work-procedure. It required little practice, and many men could simultaneously perform it in the hot-room. In this task, the energy-output as measured by the oxygen-consumption was maintained at levels of between 150 and 300 k. cal./hour, according to the circumstances. The standardization of the work-output permits the assumption that the loss of water from the respiratory tract (E_r) remains constant in an experimental series. This is true in so far as the weight-load represented by the clothing and equipment varies very little. Adjustments can easily be made in this respect.

With the work- and heat-output standardized, the comparison between two or more items under constant conditions involves, in principle, only S and E in equation 1, since sensible heat (H_s) is given by difference. The difficulties of measuring both S and E accurately have already been mentioned; the fact that S is only roughly obtained from change in rectal temperature is a limiting factor in all calculations of heat-loss factors in these experiments. Where the sweat-rate is so high as to make the measurements of unevaporated sweat unreliable because of " drip," an approximate value for E can be obtained by making sensible heat-loss (C + R) very small by carrying out the tests at a dry-bulb temperature of 95° or 96° F. i.e. near clothing-surface temperature. With (W − H) known and (C + R) regarded as a constant of small amount, and S calculated, an estimate of E can be made. This method has been used on occasion by the Unit.

The value of estimating E lies in being able to apply the index of " effective evaporation," i.e. the ratio of evaporated to total sweat-loss. In comparing tropical fabrics and in other situations, this index is of some use (the unclothed man may have an index of 70% or 80%, the clothed in some circumstances only 30% or 20% or less). The elimination of unmeasurable " drip," though useful is, however, not always possible.

By standardizing the conditions, an indirect comparison is therefore possible of the factors concerned in heat-loss from the body with different types of clothing and fabric. In the final resort, and for most military purposes, thermal study *per se* is reduced to a few easily-measurable criteria —the rectal temperature, the pulse-rate, the sweat-output, the water-uptake of the clothing and, as already mentioned, where possible, the evaporated and unevaporated fractions of the sweat-loss from the subject.

The measurement of rectal temperature is thus one of the main criteria used in clothing-tests. Its use depends also on the fact that much empirical work under controlled environmental conditions has indicated that the rectal temperature is raised proportionately to increased heat-load, whether due to increase of rate of work-output, or of load-carrying, or to changes in environmental conditions. Similarly, the pulse-rate of a particular individual bears a fairly close relation to heat-load factors.

The third important criterion, which has been extensively used, of the heat-load imposed by the clothing, is the rate of sweat-output and of unevaporated sweat-loss. The usefulness of these measurements has been established only as the type of work mentioned in this paper was continued, as well as by other hot-room work carried out by the MRC unit[3] (McArdle *et al.*, 1944-46). An increased sweat-output in some circumstances may partly be due to an increase in loss of evaporated water, but this factor can in most cases be measured, or allowance can be made for it.

[2] [1 foot = 30.5 cm.—Ed.]

[3] [See paper (*BMB* 1013) by W. S. S. Ladell in this number.—Ed.]

Where the "effective evaporation" is low, total sweat-loss appears to reflect differences in heat-load fairly reliably. More research on these and other points is still needed to establish the reliability of the simple criteria used in evaluating clothing.

The obvious utility of relatively simple measurements is that they allow a more adequate statistical control of the experiment and more variables can be given due consideration. This is of importance in clothing-experiments where other effects, such as individual differences or interaction between clothing, climates, persons and other factors, may produce effects of a magnitude comparable to that of the clothing itself.

It is also of some importance before making clothing-tests to carry out a full regime of acclimatization of the subject to the worst conditions of heat, clothing and work to be encountered in the actual tests. This requires at least two weeks of successive daily exposures (excluding Sundays) of 3 or 4 hours at least. As repeated exposure affects all the main criteria used in evaluating clothing, particularly the sweat-rate (McArdle and Weiner, quoted by Ladell, 1945) and individual differences are very great both in rate and magnitude of acclimatization (Robinson, Turrell, Belding & Horvath, 1943; Taylor, Henschel & Keys, 1943), acclimatization to the actual experimental conditions is essential. Full hydration of the subject is also usually practised.

2. Mosquito-Proofness

As the provision of mosquito-resistant fabrics was a requirement for many types of military protective clothing, methods for testing mosquito-proofness had to be devised. The "biological" test, on which main reliance was placed, was that of Sir Rickard Christophers, and was carried out at the Molteno Institute, Cambridge. This test involved exposing an area of the arm, covered by the fabric, to the bites of 200 starved *Aedes aegypti*. The number of wheals in 15 minutes was noted.

As the Unit was asked to decide on the probable mosquito-proofness of a large number of fabrics (over 60 eventually) in relation to thermal features, a rapid preliminary method was essential to differentiate at least between fabrics which were definitely mosquito-proof and those that were certainly not. A "photographic" method was devised, and consisted merely of staining a 2-inch [5 cm.] square of the fabric with an opaque dye, such as fuchsin, placing it in front of a light-source, and photographing it. This test placed fabrics into one of three categories: (i) those showing no light-penetration when stained, and which were regarded as mosquito-proof; (ii) those which showed a very few fine pinpoints of light; (iii) those which showed some fine or large light-areas and were regarded as definitely penetrable by mosquitoes.

The results of the photographic method were always subject to confirmation by the biological test. Results on 57 fabrics by both methods are available; table I shows the fabrics grouped into three classes according to each of the two methods.

It can be seen that, for discriminating between the most useful and the least useful fabrics, the photographic test is of definite value, and for differentiating between 2 classes —impenetrable and penetrable—the results are very satisfactory.

TABLE I. BIOLOGICAL AND PHOTOGRAPHIC TESTS OF MOSQUITO-RESISTANCE OF FABRICS

Biological test		Photographic test		
Degree of mosquito-resistance	Number of fabrics	Impenetrable (no light-area)	Penetrable with difficulty (very few fine points of light)	Definitely penetrable (some fine or large areas of light)
Impenetrable ... (0 wheals)	20	19	1	0
Penetrable with difficulty ... (0—5 wheals)	9	1	6	2
Definitely penetrable ... (5 or more wheals)	28	0	8	20

3. Physical Properties of Clothing and Fabrics

The physical characteristics of fabrics and clothing which are relevant to physiological performance in the tropics are the thickness, the weight per unit-area, the water-vapour resistance ("ventility"), air-permeability, water-absorption and "drying out," and the construction of the cloth. Standardized tests of these qualities have been devised by the Cotton and Wool Research Associations, with whom close contact was maintained by the MRC unit.

The thermal resistance of fabrics is dependent on the thickness irrespective of the fibre used (Rees, 1941) when measured under standardized conditions of pressure, relative humidity and windspeed. Physiological testing of fabrics has shown that increase in thickness of cloth imposes an increased heat-load as indicated, for example, by an increase in sweat-loss. Evidence is also available of the greater heat-load imposed by heavier fabrics, allowing for the effect of fabric-thickness. The relation of air-permeability to physiological effects is discussed below. The water-holding properties of a fabric, as measured by standard textile methods, are of use in indicating the probable uptake of sweat in the different layers of clothing, particularly if the fabric is found to be highly water-repellent. Details of the construction of the fabric are of interest not only in relation to thermal properties, but also to mosquito-proofness, since it is likely that the number of counts in the warp and weft are related to mosquito-resistance.

It may be said that far more systematic investigation of the relation between physical characters (particularly water-vapour permeability and water-holding properties) and physiological performance is still required, since most of the available results have been obtained, in Britain or in USA—notably by Robinson (Robinson *et al.*, 1943)—mainly during the course of *ad hoc* testing.

4. Fabrics for Action-Rig and Jungle-Suits

As the bush-shirt fabric (british cellular cloth) of the army tropical uniform is of an open construction and easily penetrable by mosquitoes, it was decided to substitute a fabric which would be mosquito-proof but which would not impose any greater heat-load than the bush-shirt and drill trousers of the usual army uniform. The effect of rendering the clothing water-repellent was one of the questions on which information was also sought. The Unit was asked, therefore, to recommend a suitable and readily-available fabric, and to investigate the particular factors governing the choice of suitable fabrics. It may be added that the United States Army insisted on mosquito-resistance as a first priority, and at the present time it still remains a requirement as a protective measure against both malaria and dengue.

For comparison with the cellular fabric of the army uniform there were available, at the time, only seven fabrics which, from their physical characters and availability, could be considered as possible substitutes for the army cellular-weave fabric or for the naval overall fabric, whose replacement was also under consideration. As shown in table II, with the exception of L 30 (an experimental type of cloth) the possible fabrics were both lighter and thinner than the cellular bush-shirt, and they were all (with one exception) impenetrable to mosquitoes. The physiological tests were therefore undertaken to discover whether the lighter and thinner fabrics would not, in fact, impose a greater heat-load in view of their greatly-reduced air-permeability.

The methods used have been described above. Fully acclimatized subjects wore suits (bush-shirt and trousers) made of the test-fabric and of identical size and pattern, together with full battle equipment. They carried out step-climbing work with rest-pauses, the energy-production over the two-hour test-period being somewhat less than that of marching at 2½ miles[4] per hour. The tests were done in " still " air-conditions, dry-bulb temperature 95° F. [35° C.], wet-bulb 85° F. [29·4° C.], air-movement less than 30 feet [9 m.] per minute, and also (with fewer suits) in a 10-miles-per-hour wind at a dry-bulb of 98° F. [36·7° C.], wet-bulb 84° F. [28·9° C.] At these dry-bulb temperatures, heat-loss by radiation and convection was at a minimum. The metabolic heat could be partitioned into (*a*) heat retained in the body (S), and (*b*) heat-loss by evaporation (E) by applying equation (1) discussed previously. S was calculated from the rise in rectal temperature, and the body-weight, specific heat, and metabolic heat being known, E could be calculated. The value for E expressed as a percentage of the total sweat-loss gave a figure for " effective evaporation " as one criterion of the heat-load, the other criteria being the rectal temperature and the total sweat-loss.

The results shown in the table indicate little or no physiological difference between the fabrics; even in the 10 miles/hour wind, the " utility " gabardine (air-permeability about 12 feet³/foot²/minute) is little different from the cellular weave (air-permeability 40 foot³/foot² per minute). American workers have confirmed this finding in a comparison of the US poplin (air-permeability 4 foot³/foot² per minute) with the cellular weave. In general, where fabrics suitable for tropical military clothing are concerned, especially in the case of thin, light mosquito-proof fabrics, it appears that a very low air-permeability does not adversely affect heat-loss. The tests done in Britain, and in America by Robinson (Robinson *et al.*, 1943), show also in general that the lighter and thinner the fabric the less the heat-load, though the differences are small. The effect of rendering fabrics water-repellent was not noticeable by physiological criteria in prolonged tests, but subjectively such fabrics are found to be quite definitely unpleasant. Against the slower and smaller uptake of moisture by the treated clothing, must be balanced the increased water-content of the underclothes, socks and boots.

The fabric recommended by the MRC unit for hot wet climate was " utility " gabardine 3170, non-water-repellent. This is a twill fabric which is not difficult to obtain.

TABLE II. COMPARATIVE TESTS OF HEAT-LOAD OF VARIOUS FABRICS

Fabric	Weight (ounces/yard²)[5]	Thickness (1/1000 inch)[6]	Still air			Wind 10 miles/hour		
			Sweat-loss (grams)	Temperature rise (°F.)[7]	Effective evaporation (%)	Sweat-loss (grams)	Temperature rise (°F.)[7]	Effective evaporation (%)
British cellular	7·97	30	1,787	2·44	29	1,360	0·95	45
" Utility " gabardine	5·21	16	1,730	2·37	32	1,354	0·85	46
US poplin	7·25	16	1,729	2·65	31			
Naval twill	7·11	19	1,777	2·50	30	1,379	1·08	45
L 24	6·10	14	1,790	2·30	31			
L 30	9·15	21	1,800	2·41	29			
No. 2† drill	6·92	25	1,862	2·69	28			

† Penetrable to mosquitoes with difficulty.

5. Some Features in Design

As mentioned at the outset, the clothing-assemblies investigated by the Unit, apart from regular military clothing, were often of a specialized kind. Some of these required the wearer to operate in climates of a wet-bulb temperature near 80° F. [26·7° C.], in bulky and quite heavy clothing made of fabrics impermeable to air, and in some cases the head was enclosed within a helmet.

In such situations, it was often necessary to stipulate the limiting environmental conditions in which the man could be expected to perform his task, and also to attempt modifications of the design to reduce the heat-load. The two most useful measures usually explored in such cases were: (i) wetting the outside of the clothing and thus maintaining the surface-temperature of the clothing-assembly near to the wet-bulb temperature of the air; (ii) the possibility of blowing in a relatively-large volume of outside air or a smaller volume of conditioned air, i.e.

[4] [1 mile = 1.609 km.—Ed.]
[5] [1 ounce = 28 g.
1 yard = 0.9 m.—Ed.]
[6] [1/1000 inch = 0.0254 mm.—Ed.]
[7] [To convert °F. to °C. subtract 32 and multiply by 5/9.—Ed.]

air either cooled or dried; (iii) a combination of both.

The first measure, simple as it is, often produces quite marked improvement, as shown some years ago in the case of gas-protective clothing by Crowden (1938). The fact that, in certain military operations, the protective clothing could be wetted in the sea, was in some cases the main circumstance making its use possible in conditions of high dry-bulb temperature and solar radiation.

The second method is applicable, of course, only where a blower, and if necessary a refrigeration-unit or a supply of dry air, are available; the provision by these means of a "micro-climate" under the clothing, which prevents the rectal temperature rising above, say, 99·5° F. [37·5° C.], may often require only a small quantity of ambient air, providing that it is fairly well distributed under the clothes and the wearer does not perform excessive work.

Some experiments from a number carried out by J. C. D. Hutchinson may be quoted to illustrate the effects of these procedures. The suit was totally impermeable to water-vapour, and the wearer performed light work. Table III makes clear the difference in heat-load as a result of treating the suit as described, using the physiological criteria already discussed. Air movement was "still"—about 50 feet/min.

A problem encountered not infrequently is the case where the clothing which may be comfortable in the tropics in one situation may quickly become too cool in another set of circumstances. Thus, clothing may be too cold for prolonged immersion in a tropical sea at night, while quite suitable ashore; or clothing suitable for the water may be too hot for hard work ashore, even if wetted. Similarly, in the RAF, pilot's clothing before flight may be quite uncomfortable, especially with high radiant-temperatures from the surroundings, and yet not be warm enough when flying. The obvious expedient of ventilating the clothing with cool or warm air as necessary illustrates the paradoxical situations that one may encounter in the tropics.

TABLE III. EFFECT OF WETTING OR VENTILATING PROTECTIVE CLOTHING WORN AT HIGH WET-BULB TEMPERATURES

Environment		Treatment given to suit	Sweat-loss (cm.³/min.)	Maximum rectal temperature (°F.)	Sweat in underclothes (cm.³)	Pulse-rate taken standing after light work
Dry-bulb temperature (°F.)	Wet-bulb temperature (°F.)					
90·0	82·0	dry	6·33	99·3	400	94
		wetted	2·28	98·9	120	84
		wetted and with blower	1·37	98·8	94	84
100·0	87·0	dry	11·0	100·0	608	107
		wetted	9·1	99·8	606	93
		wetted and with blower	6·4	99·3	250	89

6. Conclusion

From the war-time *ad hoc* work of the Medical Research Council Climatic Unit, in dealing with military clothing-problems, outlined above, the main features of physiological testing of tropical clothing may be fairly well illustrated. The methods necessary in principle and in practice for the assessment of the heat-load have been discussed, and certain of the more important fabric-properties, particularly that of mosquito-proofness, are described. Consideration is given also to certain devices used in dealing with the excess heat-load of specialized clothing-assemblies.

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ANTHROPOMETRIC PROBLEMS IN THE ROYAL AIR FORCE

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1 Body-measurements
2 Measurements of man and machine
3 Information on the physical development of the population derived from measurements of heights and weights
4 Body-measurements and crew-duties
5 Age-curves for height and weight
6 Other applications of anthropometric research

Body-measurements are of various kinds, and knowledge of their variation for groups of men may be of military significance in various ways. The questions to which such knowledge is applied can be divided into two groups according to whether they are of medical interest, or whether they concern matters which are not of a medical nature. During the war, anthropometric research carried out in the Medical Directorate of the Air Ministry was concerned chiefly with non-medical problems. This was so because workers at the former RAF Physiology Laboratory, now the RAF Institute of Aviation Medicine, were charged with promoting the safety, welfare and efficiency of all flying personnel in the Service from a general, as well as from a medical, point of view. Such matters concern selection on medical grounds, the maintenance of physical fitness, and examination of the physiological effects of the exceptional conditions to which airmen may be exposed. They also involve consideration of more mundane questions, such as the design and fitting of the special clothes and personal equipment worn by aircrew, the lay-out and dimensions of the restricted spaces in which they must be able to operate with comfort, and means of rapid escape from aircraft in emergencies.

There was no lack of practical problems relating to body-dimensions of aircrew. I was occupied with them during the last year of the war under the general direction of Air-Marshal Sir Harold Whittingham, who was Director-General of the Medical Services of the Air Ministry at the time. The first need was for information regarding variation in the body-measurements of aircrew. This was obtained from several sources. Two surveys providing the measurements required were carried out. One was of 2,400 recruits for flying duties, and another, undertaken primarily to obtain information required for sizing clothing, was of 520 flying personnel in training. The measurements taken were of an unusual kind designed to assess the space occupied by the body in different positions, rather than the proportions of its anatomical parts.

1. Body-Measurements

Length-measurements such as stature, sitting height, the lengths of the arms and legs, and so on, were taken with the aid of the measuring board shown in fig. 1. The two wings of it are fixed so that they are perpendicular to one another. Horizontal and vertical scales with half-inch [1·27 cm.] intervals are marked on them, the origins being the line where the two wings meet and the plane of the floor. The subject sits, or stands, in a specified position, and a triangular block is brought into contact with one terminal of the length

FIG. 1. APPARATUS USED IN MEASURING BODY-LENGTHS

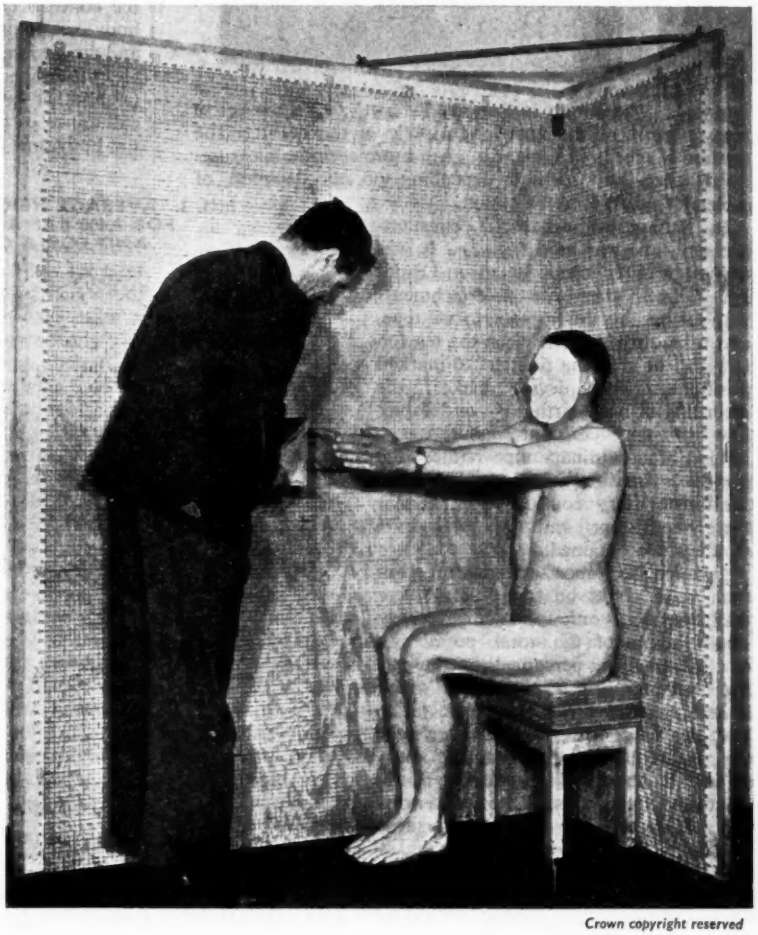

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FIG. 2. MEASUREMENT OF CHEST-GIRTH WITH A CONSTANT-PRESSURE TAPE

required. The length is then read directly, as a projective measurement, on the appropriate scale of the board. The method is speedy in use and it gives more accurate measurements than any method depending on the location of skeletal " points " by palpation.

In finding body-girths, a constant-pressure tape was used (fig. 2). It was devised by my colleague Squadron-Leader J. C. Gilson. There are two attachments with springs in them fastened to the tape, and a reading is taken when the tension is sufficient to bring pointers to marked positions. This device makes the recording of body-girth easy and rapid. Use of the constant-pressure tape instead of an ordinary tape reduces the personal equation in measuring, say, chest-girth, very considerably, so that more consistent and more accurate readings are obtained.

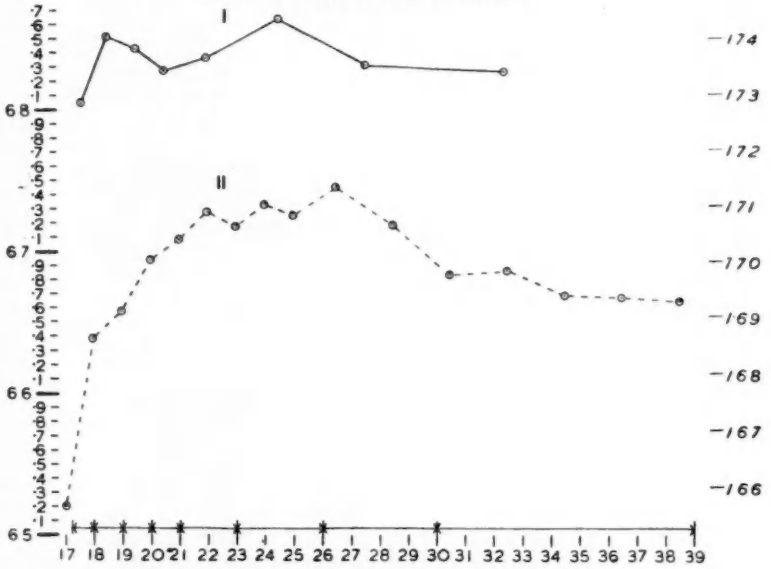
Detailed body-measurements taken in such ways could be found—and were really required—only for a comparatively small sample of the total population of all RAF flying personnel, but heights and weights were available for much larger numbers of the men. For purposes of control, height and weight happen to be the best pair of measurements that could be chosen. Body-lengths—such as those of the trunk, arms and legs—can be predicted most accurately from height, while girths of the trunk and limbs can be predicted better from weight than from any single girth or other measurement.

These data provided the essential basic knowledge required in dealing with problems associating a number of men of various sizes and shapes with spaces in which they have to operate, or with clothes or special equipment they have to wear. After the data had been reduced, the measurements could provide an answer to a question of this kind: if pilots were more stringently selected on account of size—if all less than 67 inches [170 cm.] in height were excluded, for example—what would be the distributions of other measurements, such as arm-length and leg-length, for the selected group ?

2. Measurements of Man and Machine

But many practical problems dependent chiefly on variation in body-size could not be answered without obtaining further information. The body-measurements available relate to static bodies. A fighter-pilot in flight, say, has to be constantly moving his arms and legs to operate controls, and his head and body to scan instruments and his surroundings. By themselves, the body-measurements cannot give any precise answer to the question of what the major dimensions of a cockpit should be and of where the controls can best be placed. It is clear, too, that the body-measurements alone cannot tell what the best shape and dimensions are for an escape-hatch in a bomber when the aircraft-designer requires the hatch to be as small as possible. Or another factor may be involved, such as strength and endurance of the legs which will depend on the position of the body and other conditions.

FIG. 3. AVERAGE HEIGHTS AT DIFFERENT AGES FOR 2,400 RAF AIRCREW RECRUITS AND FOR A CIVILIAN SERIES



Abscissae : Age in years (RAF age-groups shown by X)
I = RAF series
II = civilian series of employed men, 1929-32
Ordinates : Right side : height in cm.
Left side : height in inches

Such problems concern bodies functioning in particular ways. They can be investigated satisfactorily only by carrying out experimental investigations. In a particular case, an experiment has to be arranged reproducing the conditions of the problem, and observations have to be taken on a number of subjects. Their size will be one of the factors involved, and hence it is necessary to measure them. By relating the body-measurements of the subjects to those available for the total group considered—which may be all flying personnel, or pilots only, or air-gunners only—it is possible to obtain conclusions for that total group. Such questions are too specialized to be of general interest, and usually there are no medical considerations relevant to them. However, the extensive records of the heights and weights may at least be of indirect medical interest.

3. Information on the Physical Development of the Population Derived from Measurements of Heights and Weights

Fig. 3 shows average heights at different ages for 2,400 accepted candidates for flying duties measured in 1942, and for a larger civilian series measured before the war. No limits of height were applied to the aircrew-recruits, and the fact that they are taller at all ages than the " employed men " may be attributed to medical and social selection. From records collected at various dates, it has been found that there are appreciable differences between the average heights of series of men representing different social classes. A more interesting point is that the aircrew-recruits aged 18 had an average height as great as that for any later ages. Actually there are no statistically-significant differences between the means for any age-group from 18 onwards.

The situation has been found to be the same for other series of flying personnel and for ground-staff, these records being for a total of about 30,000 men. For every series the average height is found to be as great for age 18 as for later ages. To anyone familiar with the records of heights of british men in pre-war years this must appear to be a remarkable fact. All the earlier series representing the british population in general which are long enough to provide good statistical evidence give average heights showing appreciable increases up to some age between about 23 and 25 years. The civilian series in fig. 3 actually shows the greatest average for age 26, but the maximum had almost been reached by age 22. This is quite a marked difference from the attainment of maximum height at age 18 found for the RAF series.

It may be suggested that, owing to the way they are selected, a group of men accepted for one of the fighting Services may give a distorted picture of an age-curve. But this had not been suspected previously, and there are no height limitations applied to recruits in general in Britain. The heights of 200,000 recruits reported after the war of 1914–18 show a maximum average at age 25. In fact there seems to be no reason why the conclusion that maximum height is normally reached at age 18 to-day should not be supposed true for the total male british population. If this be accepted, then there is good evidence to show that skeletal maturity is now attained normally some five years earlier than it was a few decades ago.

During the twenty years between the two wars, much attention was paid to growth in children. It was shown repeatedly that, at any particular age, they were becoming decidedly taller and heavier on the average. Controlled experiments showed that the more rapid growth of the children could be attributed, partly at least, to improved nutrition, which might take the form of additional milk. It was commonly stated that british people in general were increasing in size owing to better feeding, the implication being that when they were fully grown the children who were growing up more quickly would be larger, on the average, than their parents. In fact there was no good direct evidence favouring that contention, because there were no good series of measurements of heights and weights for ages between 17 and 25 years. Nearly all the series were for ages below 17. That gap is now filled by records collected during the war.

For RAF ground-staff the average height without boots is close to 67·7 inches [172 cm.], and for the more stringently selected aircrew it is nearly an inch [2·54 cm.] greater. Making a slight allowance for the effect of selection on medical grounds, it is reasonable to conclude that for the total british adult male population the average stature to-day must be close to 67·5 inches [171·4 cm.]. Records collected during the war for large numbers of men in the army and for civilians suggest that this estimate must be close to the true value.

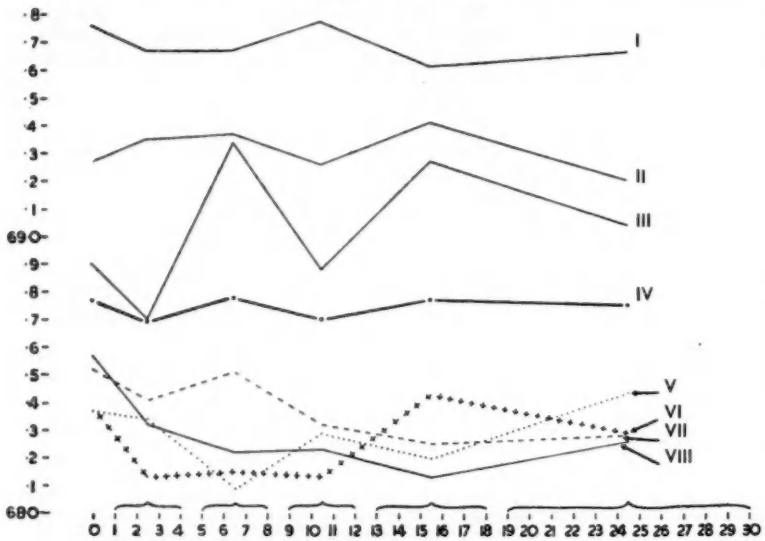
Fig. 3 shows that the series of employed men for ages 22 and over had an average height about 67 inches, but there is reason to believe that, for the general population about 1930, the average must have been nearer to 67·5 inches. Surveys carried out in earlier years back to about 1860 lead to the same conclusion, and there is no good evidence for earlier times. In the past 75 years the average stature of british men seems to have remained remarkably constant, and there is certainly no clear indication of any secular increase in recent years. There has been a decided change in the age at which skeletal maturity is reached and this is an interesting point. We have been growing up more quickly without becoming larger when fully grown. Before long we may know whether the secular change in the growth-rate which was manifested between the two wars was maintained throughout the second war, or whether conditions then reversed the process.

4. Body-Measurements and Crew-Duties

Fig. 4 is based on measurements of 8,000 personnel who were operating in Bomber Command in April, 1944. Average heights are shown for crew-duties separately and, for each crew-duty, points are given for different series distinguished by the number of sorties flown by the men. There is seen to be a clear separation of the crew-duties. This is partly due to deliberate selection for height applied when the men were allocated to particular duties. There was a minimum height-limit of 64 inches [162·6 cm.] for pilots and a maximum height-limit of 72 inches [182·9 cm.] for air-gunners. Otherwise the crew-duties were not selected on account of body-size.

The clear stratification, as it were, of the average heights for crew-duties, other than those of pilot and air-gunner, may be attributed to a process of selection not directly involving height. Starting with a group of recruits accepted for aircrew training, those who were to become pilots, navigators, and bomb-aimers were selected first. On the average, these would be the better-educated, so the sorting-out gave a separation something like that between social classes, which are known to be distinguished by average heights.

FIG. 4. AVERAGE HEIGHTS FOR DIFFERENT CREW-DUTIES (BOMBER COMMAND) RELATED TO THE NUMBER OF SORTIES FLOWN BY THE MEN



Abscissae : number of sorties flown

I = pilots
II = navigators
III = bomb-aimers
IV = all aircrew
V = rear-gunners
VI = flight-engineers
VII = middle-upper gunners
VIII = wireless operators

Ordinates : average height in inches
[1 inch = 2.54 cm.]

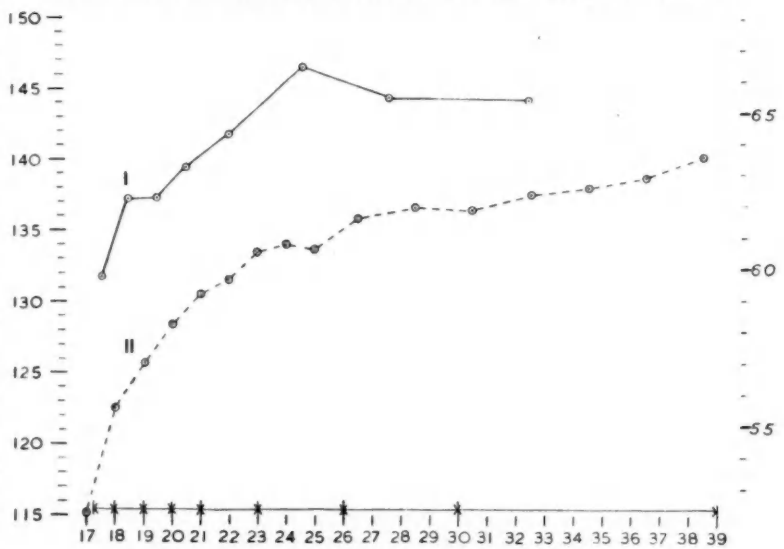
Heights of series for groups of men who had flown different numbers of sorties were examined for a particular purpose. If either extremely large or extremely small men had been so handicapped in performing their duties that their chance of survival was less than that for men of normal size, then this might have resulted in the distributions of heights being slightly different for airmen starting operations and for veterans. In fact, no suggestion was found, judging from the measurements of heights for large numbers of aircrew, that body-size was in any way related to the chance of survival. It can be seen from the diagram that there is no suggestion of a trend towards either increase or decrease in the average heights for any crew-duty with increase in the number of sorties flown.

Heights were involved in another enquiry concerning a particular type of aircraft. It was suspected that small pilots were at a disadvantage in operating this type because it was rather more difficult for them to manipulate its controls. The heights were obtained of a number of pilots who had had accidents while flying the aircraft in question. Small heights were found to be no better represented in this series than among pilots in general, so no confirmation was obtained in that way of the belief that small pilots were handicapped in controlling the aircraft in an emergency.

5. Age-Curves for Weight

Both heights and weights of large numbers of aircrew were obtained. Fig. 5 shows the age-curves for weight for aircrew-recruits and a civilian series. At every age the RAF series shows a greater average height than the employed men (see fig. 3), so the separation of the two weight-curves is not surprising. They are distinguished in another way. All large civilian series show a steady increase in average weight with increasing age up to and beyond age 40. A parallel increase is usually found for Service series up to about age 30, but for later ages there is either a distinct slackening in the rate of increase, or, possibly, as for the recruits, a slight decline. Physical fitness after 30 is not indicated by increase in weight.

FIG. 5. AVERAGE WEIGHTS AT DIFFERENT AGES FOR RAF AIRCREW RECRUITS AND FOR A CIVILIAN SERIES

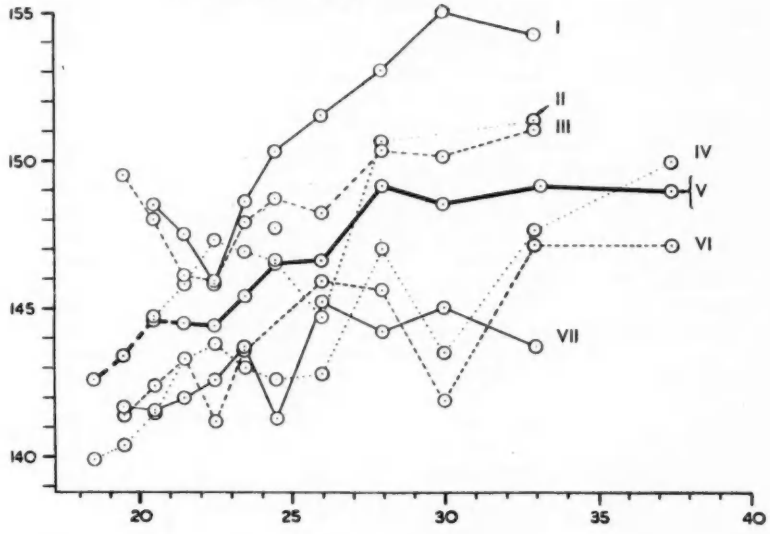


Abscissae : age in years (RAF age-groups shown by X)
I = RAF series
II = civilian series of employed men, 1929-32

Ordinates : Right side : weight in kg.
Left side : weight in pounds
[1 pound = 0.45 kg.]

FIG. 6a (UPPER), 6b (LOWER). AVERAGE WEIGHTS FOR DIFFERENT CREW-DUTIES (BOMBER COMMAND) AND DIFFERENT AGES

6a. Observed weights



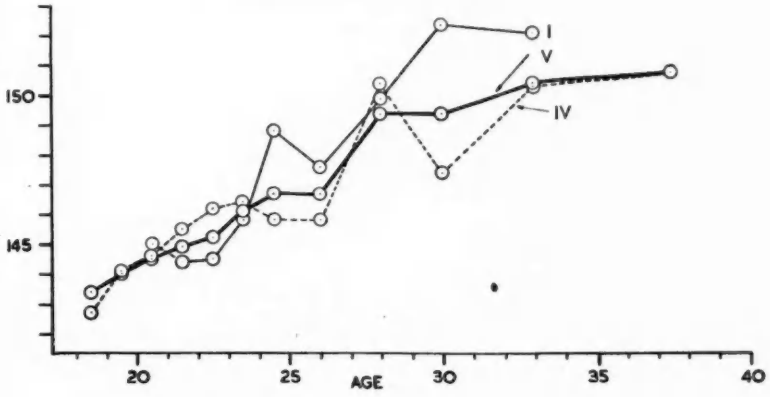
It is seen from fig. 4, based on measurements of flying personnel of Bomber Command, that there are substantial differences between the average heights for different crew-duties. Some, but not all, of these differences are due to deliberate selection in applying height-limits. The age-curves for weight (fig. 6a) also distinguish the crew-duties and show them in the same order. It is more interesting to compare average weights for the series after allowance has been made for the differences in height. Fig. 6b shows the age-curves for weight standardized to a height of 68·5 inches [174 cm.] for pilots, air-gunners and all aircrew. For the constant height the pilots are seen to have rather greater average weights at most ages, but the distinction is by no means marked. Allowing for differences in height, it can be said that crew-duties are hardly distinguished from one another on account of weight.

Fig. 7 shows a number of age-curves for weight for air-crew series, all averages used being standardized to a height of 68·5 inches. The two lowest curves are for RAF series, the lowest being for the 2,400 aircrew recruits measured in 1942, and the one above it is for the 12,000 personnel of Bomber Command measured two years later. These two series are scarcely distinguished by heights, but there is a clear difference between the average weights for them. It is not difficult to find a plausible explanation of the difference. Most of the recruits were civilians until a few days before the time they were measured. All the operational aircrew had been flying personnel for more than two years and they had been fed—as they fully deserved to be—as well as any people in Britain.

The other three age-curves shown in fig. 7 are for Dominion series of aircrew who were in training or were operating in Bomber Command in 1944 when they were measured. The totals, in round numbers, were 4,000 for the canadian, 1,600 for the australian and 550 for the New Zealand series. The average heights are practically the same for the australian and New Zealand as for the RAF series, and the average height of the Canadians is about 0·5 inch [1·27 cm.] greater. At all ages the Dominion series are clearly separated from the british series by the average weights after allowance has been made for differences in height. This situation may be partly due to other factors affecting the selection of the Dominion aircrew, but it seems to me to be probable that it is due primarily, at least, to differences in nutrition. It is not unlikely that the superiority in weight of the New Zealand airmen, the good health-statistics, and the high consumption of dairy-produce in New Zealand are all related facts.

Such questions are chiefly of academic interest. The heights and weights of aircrew collected during the war have been used to serve a more practical purpose. They have given a new age-height-weight table suitable for use

6b. Weight standardized to height 68.5 inches



Abscissae : Age in years

I = pilots
II = bomb-aimers
III = navigators
IV = gunners
V = all crew-duties
VI = flight-engineers
VII = wireless operators

Ordinates : Weight (nude) in pounds

in medical examinations of candidates for flying duties. In constructing this it was assumed that the medical officer will attach little importance to weight unless it is clearly exceptional. For any particular age and height the average weight is given and also two other weights. The first of of these is such that only 1% of candidates will be expected to have lesser weights, and the second is such that only 1% will be expected to have greater weights. A range of weights within which 98% of candidates will be expected to fall is thus defined for each age and height.

6. Other Applications of Anthropometric Research

Anthropometric research is not limited to height and weight. It may concern many of the medical and other tests used in selecting Service personnel for particular duties, and many of the enquiries relating to the equipment they use and the conditions under which they operate. The following remarks refer less to any part I played in investigating such questions than to the work of others and to research which might be carried out in future.

After a new piece of personal equipment has been designed—say, an oxygen-mask or a flying-suit—a certain number will be made and circulated for field-trials. Those who use the new equipment will be asked to return a questionnaire giving their opinions of its suitability. After these have been examined it may be decided that the equipment is unsuitable, or that it should be modified in certain ways before large numbers are made and the equipment is adopted for general use. Validation by field-trials is required before that step is taken.

Ideally, at any rate, it should be possible to validate medical and other tests of personnel. One may attempt to do this in various ways. For example, a new laboratory test of night-vision is devised. This may be applied to a number of subjects, giving a grading of them for acuity of night-vision. On a second occasion the test may be applied again to the same series of subjects, and this will grade them in a rather different way. A comparison of the two gradings will give a measure of the reliability of the new test which will show whether it is more or less reliable, judged in that way, than earlier tests of visual acuity at night. This may be the first stage in the testing of the test. The second stage might be the collection of scores for the same series of subjects in a field-trial, such as spotting objects in the open at night. These scores could be compared with those for the laboratory-test. A third stage might be of a different kind. For night-fighter pilots in wartime, say, scores for the laboratory-test could be related to the number of enemy-aircraft shot down, making allowances for the number of hours each pilot had flown and what his opportunities were. It would not be surprising if very little association between the two assessments was found, since many factors besides acuity of night-vision must determine a pilot's score in shooting down enemy-aircraft.

Different methods have to be used, of course, in assessing the validity of different kinds of measurements, but for all tests it must always be possible to estimate reliability by repeated application to the same series of subjects on two or more occasions. Several of the tests used in Service medical examinations have themselves been tested in this way during the war. The general conclusion seems to be that nearly all tests of the functioning of the body or of the mind show a low degree of reliability. When any one is repeated the grading of a series of men is nearly always found to be substantially different from the grading obtained on the first occasion. It has been shown for some tests that if they are applied repeatedly on different days the average scores may have far greater reliability than single observations. The obvious explanation is that physiological states fluctuate from day to day, from hour to hour, and even from moment to moment, though the levels about which they fluctuate may be characteristic for individuals. There is nothing new in this conclusion, of course, but recent research has emphasized the point that due regard must be paid to it before good validation of several tests commonly taken in medical examinations can be expected.

In all three Services the conditions of modern warfare have necessitated the selection of men who are exceptionally fit for particular duties. The need is for tests which will discriminate grades of fitness, though this can have no precise meaning

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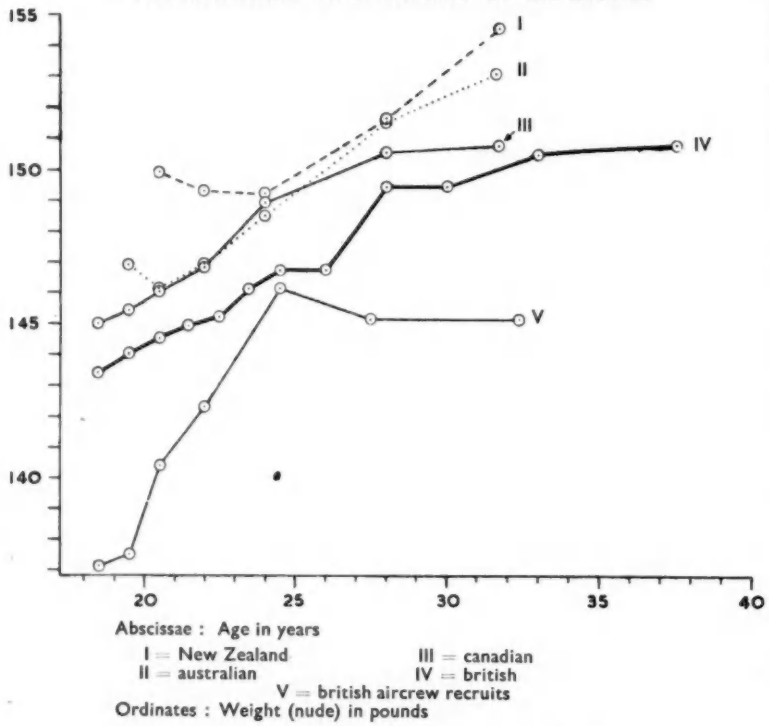
FIG. 7. AVERAGE WEIGHTS AT DIFFERENT AGES FOR AIRCREW SERIES, STANDARDIZED TO A HEIGHT OF 68.5 INCHES



SOME ANATOMICAL AND PHYSIOLOGICAL PRINCIPLES CONCERNED IN THE DESIGN OF SEATS FOR NAVAL WAR-WEAPONS

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Prolonged standing at work is probably one of the commonest causes of avoidable discomfort and fatigue, but until recently the provision of seats has been considered unnecessary and even undesirable, for seats have been thought to encourage laziness and thus, in the armed forces especially, it has been traditional for the operator to stand at his work. However, employers and naval officers have now been persuaded that seats not only afford a valuable method of combating fatigue and thereby increasing capacity for work, but also enable work to be performed with greater accuracy. This is particularly important now that designers are producing mechanisms capable of precision which is limited only by the performance of the operator. Operators should, therefore, sit at their work wherever practicable, but the design of the seat must be based on certain anatomical and physiological principles if the maximum possible efficiency is to be obtained.

The seat must support the body in a normal comfortable position and must be so placed that the operator is in the optimum relation to his work. To arrive at the best design, close co-operation is necessary between the anatomist and the seat engineer, a factor which has been neglected in the past.

This report is primarily concerned with the design of seats for use in naval optical-sights. Nevertheless, as a result of laboratory tests, and from the information obtained from " users," certain general principles can be formulated which can equally well be applied to civilian problems.

1. PRINCIPLES AND REQUIREMENTS

The chief requirements of an ideal seat for use with naval war-weapons are as follows :—

a It must accommodate at least 90 % of individuals of different body-dimensions in the most efficient position.

b It must permit the attainment and maintenance of the maximum degree of body-stabilization.

c It must allow the operator to maintain a sitting-position for periods of duty up to four hours without undue discomfort or fatigue, and must allow for an alert and a relaxed position.

d It must combine lightness with mechanical efficiency, withstand very severe usage, and be weatherproof.

A. Accommodation of 90% Range

The seat must accommodate at least 90% of all naval personnel in the most efficient sitting-position but, at the same time, it must occupy the least possible space. It is generally agreed that to consider the remaining 10%, composed of persons at the extremes of the range of anthropometric measurements, would lead to difficulties of design which would outweigh any advantage gained by the increase in the number of potential operators. In order to accommodate persons within the 90% range, the position of the seat must be precisely related in each person to the foot-rest, so that the legs are held in the correct position, and to the eyepieces of the binoculars, so that the eyes are on a level with the optical axis of the sighting-apparatus. To allow persons of different statures to fit themselves to the seat accurately and rapidly, a simple single control to allow simultaneous adjustment of the foot-rest to the seat, and of the seat to the eyepieces of the sight, is advantageous.

It is also of importance that, in the design of the machine, sufficient clearance should be allowed between the body of the operator and the surrounding structures, so tha tthe operator is allowed a certain degree of unhampered movement. If this is not done, part of the surrounding structure may press uncomfortably on the operator, or he may have to assume an awkward posture in order to avoid the pressure. In extreme cases, although the design of the seat may be satisfactory, it may be impossible to man it because this point has not been considered.

B. Body-Stabilization

A means of body-stabilization is essential in order to counteract the movements of the ship, gun or director while observations are being made and manipulations carried out.

ANTHROPOMETRIC PROBLEMS IN THE ROYAL AIR FORCE

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unless an answer is given to the question: fitness for what? In the RAF the answer is fitness for flying duties. Excellence in a number of qualities may then be demanded, including ability to respond well to certain quite exceptional conditions encountered in military aviation. A close approach to the flying conditions can be produced on the ground with a decompression-chamber which reproduces the atmospheric environment at high altitudes, and with a centrifuge which subjects a person in it to acceleration and sudden changes in speed. It has been found that fit subjects who undergo such tests vary greatly in their responses. So far no physiological tests have been found which would make it possible to predict an individual's response to the unnatural conditions, and there is scope for research in seeking tests which would do so.

In conclusion, I should like to say a word about the possibility offered by the medical records kept by the Services in examining the validity of medical examinations. A man starts his military career by having one medical examination and he ends it by having another, while he may have others in between those extremes. If unfit for duty, he will be examined by a medical officer at once and a complete record of any illnesses he may have will be kept. There is no other section of the community for which such complete medical records are available. They make it possible to relate the examination as a whole, or particular tests, to medical histories in general, or to a group of men having a particular disease. There is no lack of scope for research in this field.

Whatever method is adopted, the arms must be left free to operate controls and the mobility of the neck and trunk must not be restricted for sighting-movements. Body-stabilization by the use of a retaining mechanism is undesirable, for it is liable to limit the movement of the arms and trunk and it also unnecessarily adds to the manipulations to be performed by the operator, when he takes up his position, which he may have to do rapidly in the dark. Furthermore, the feeling that the harness, even though it may be fitted with a quick-release catch, may hinder rapid escape, has an undesirable psychological effect. It is, therefore, probable that body-stabilization should be effected by the operator himself with the minimum of muscular effort by counter-pressure between feet against a foot-rest and back against a back-rest.

C. Reduction of Fatigue

i. *General Considerations*

A correctly designed seat can help to reduce the fatigue of the operator to a minimum by allowing him to sit in a good position. This is a position in which the different segments of the body are balanced vertically upon one another, so that the weight is borne mainly by the bony framework with a minimum of effort and strain on muscles and ligaments (Bowen, 1928) and no arteries or nerves are subjected to excessive pressure. Clinical evidence shows that a close correlation exists between health and good posture (Brown, 1917; Jones, 1933; Steindler, 1935; Hansson, 1945), and that bad posture is liable to cause disabilities involving the skeletal, muscular, circulatory and digestive systems (Goldthwait, 1941). Moreover, it has been shown that corrections in posture increase alertness, vigour and endurance (Osgood, 1931) and improve the circulation and respiration of most people (Laplace & Nicholson, 1936). The improvements occurring from a well-poised body are due to the fact that the various organs are allowed adequate space in which to perform their normal function (Bowen, 1928; Goldthwait, Brown, Swain & Kuhns, 1934; Goldthwait, 1935, 1941). It must be noted, however, that there is no one correct posture for all individuals (Appleton, 1946), because the normal range is large. Thus the design of the seat must be such that it imposes on the operator the best average position.

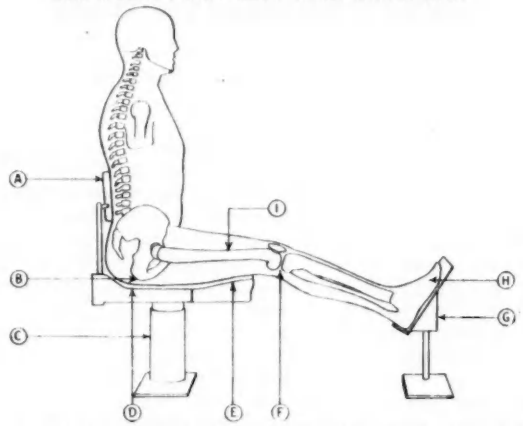
When rest-pauses can be taken, even if the pause lasts only a minute, the operator must be able to change his posture, thereby promoting the circulation through fatigued muscles (Vernon, 1922). This can be effected by allowing the operator to slide forward in his seat and lean against a back-rest. This has the added advantage that some of the body-weight is distributed to the back, thus relieving the pressure on the skin over the buttocks. Even a few minutes in a reclining position provides more rest than can be obtained by small changes in the upright position (Gilbreth & Gilbreth, 1919).

ii. *Principles of Design*

In order to realize these ideals, the design of the seat-cushion, foot-rest, and back-rest must be considered in detail:

a. Seat-cushion should be wide enough to accommodate subjects of maximum dimension within the 90% range wearing thick winter-clothing, as well as allowing a certain amount of lateral movement. Its depth from front to back should be sufficient to afford light support for the thighs almost to the hollow of the knee (Hebestreit, 1930), but the thighs must not press heavily against the front edge of the cushion, for this may lead to discomfort and possibly to interference with the blood-supply to the legs. The cushion must not project so far forward that it prevents the free movement of the legs. It is desirable that the part of the cushion supporting the ischial tuberosities should be flat and disposed horizontally. The main advantages of this are that:—

FIG. 1. "IDEAL" SEAT FOR EFFECTING BODY-STABILIZATION BETWEEN FOOT-REST AND BACK-REST



A Back-rest fits lumbar region. Note its depth and the position of the pivot
B Ischial tuberosities bear most of the weight
C Seat adjustment
D Back of cushion firm and resilient
E Front of cushion soft and resilient
F Knee-angle 160°
G Foot-rest moves upwards and towards seat to accommodate smaller persons
H Foot at right-angles to leg
I Thigh horizontal

FIG. 2. SEAT FOR USE IN NAVAL WAR-WEAPONS

Note that the seat is *not* correctly adjusted compared with fig. 1

i. it allows accurate and reproducible measurements to be made, for instance, those between the top surface of the seat-cushion and the optical axis of the sight, and between the top surface of the seat-cushion and the back-rest ;

ii. it permits the operator to change his position readily during periods of relaxation. This gives periods of rest to different muscles and thus prevents strain of any individual muscle-group, and also allows the transfer of pressure from one part of the buttock to another during prolonged watches, thus minimizing fatigue and discomfort ;

iii. the operator is able to slip forward on the cushion as may be necessary when sighting at high angles, and

iv. access to and escape from the seat are facilitated.

The cushion should be resilient (Hebestreit, 1930 ; Kindeberger & Atwood, 1935 ; Beal, 1945), but the resilience should be only in a vertical plane, as any lateral or antero-posterior sway will lead to instability and consequent difficulty in keeping the eyes applied to the binoculars. The extra muscular activity thus necessitated will increase the liability to fatigue. The resilience should be of such a degree that the body-weight, taken on the buttocks, is distributed over as large an area as possible, with the proviso that the maximum pressure remains over the ischial tuberosities. This last consideration is of importance as the ischial tuberosities are the normal anatomical supports of the seated subject, and they serve not only to protect the adjacent soft parts from undue pressure, but the skin over these bony eminences, unlike that surrounding it, is specially modified in blood-supply to withstand prolonged pressure (Edwards & Duntley, 1939).

If the seat-cushion is too soft, the excessive transfer of pressure to adjacent parts may cause serious discomfort. The resilience should be such that the variation of the degree of compression of the cushion does not exceed 1 inch (2.54 cm.) with persons of different body-builds. This is particularly necessary in seats which have a simultaneous adjustment of seat-height and foot-rest position, as this adjustment is based on the fact that there is a close correlation between leg-length and sitting-height. If the range of compressibility is greater than 1 inch, the correct relation between the foot-rest, seat and sight can no longer be maintained.

Initially, it had been hoped that, as there is a fair correlation between height and weight in the individual, a direct relationship would be found between the sitting- or standing-weight of the individual and the degree of compression of the cushion, so that allowance could be made for the variation of compression in different persons in the seat-adjustment. Practical tests showed that no direct relationship existed. The reason for this is that compression depends upon several variable factors in addition to the weight. These are the area compressed, and the distribution of the weight over this area ; variations in the resilience in different parts of the cushion ; and the attitude of the subject and his degree of relaxation. The resilience should remain of the same degree after prolonged use and the cushion should not assume a permanent change of shape. The design of the cushion should be such that all cushions to be fitted to the same model of ocular sight can be manufactured with a standard degree of resilience. A resilient cushion helps to eliminate transmitted vibrations, which are one of the causes of unnecessary fatigue (Gilbreth & Gilbreth, 1919 ; McFarland, 1941).

b. Foot-rest should be placed so that, at the ankle, the foot is maintained at right-angles to the leg, for, in this position, at rest, both the anterior and posterior groups of leg-muscles are relaxed and, when exerting pressure, both groups are contracting equally and no undue strain is thrown on either group. The relation of the seat to the foot-rest must also be determined accurately, so that, when the seat-height is adjusted to the ocular height, the knee-angle will be such that maximum counterpressure can be developed. In addition, the foot-rest must be long enough to accommodate the largest foot, and wide enough to accommodate the widest foot in the optimum position for exerting pressure. A heel-rest should be provided to prevent the feet slipping off the foot-rest.

c. Back-rest should afford comfortable resistance against which the body can be braced in order to keep it steady (Müller, 1936 ; Koch, 1941). At the same time, it must not restrict extension and backward bending of the spine or movement of the arms. A complete support for the back is not possible, owing to the limitations of space and weight, and also owing to the restriction this would impose on the movements of the spine. This being so, the most efficient support for the back can be provided by a back-rest fitting accurately into the lumbar hollow (Hebestreit, 1930). This allows free mobility at the thoraco-lumbar junction of the spine, where the greatest degree of spinal movement occurs (Gallois & Japiot, 1925 ; Bowen, 1928). If the rest is placed higher than this, movement of the spine is restricted, and the rest tends to press uncomfortably against the thoracic curvature, leading to a flattening of the lumbar hollow and a faulty sitting-position with consequent early onset of fatigue.

For optimum efficiency, the pressure applied to the back-rest must be distributed equally over as large an area as possible. If pressure is localized to a small area, it will cause discomfort and even pain, and is therefore liable to limit the degree of counterpressure which can be developed and so render body-stabilization inefficient. In order to realize these requirements, the transverse curve of the back-rest must conform to the anatomical curvature of the lumbar region, and the dimensions of the back-rest should permit the accommodation of individuals of varying sizes. The rest should be suitably padded and have broad rounded edges. The rest should be so pivoted about a transverse axis that it automatically adjusts itself to fit the different slopes of the back in different people when sitting erect, and to the changing contours of the back during sighting-movements. It should be collapsible, so as to allow easy access when the seat has to be entered from behind.

Originally it was recommended, with the idea of minimizing fatigue, that a lower (lumbar) and an upper (shoulder) rest should be incorporated in all seats which have to be occupied for long periods, and also in seats to be occupied by personnel subjected to alternating periods of activity and rest. Practical tests have shown, however, that the upper rest is unnecessary when the seat is provided with a correctly designed lower rest.

D. Mechanical Factors

Apart from the anthropometric, anatomical and physiological requirements outlined above, there are mechanical

factors which must be taken into consideration. The individual components of the seat-assembly must be capable of withstanding very severe usage under extremes of climatic conditions. They must be durable, weather-proof, sea- and freshwater-proof, oil-proof, rot-proof, termite-proof and fire-proof. The construction of the seat must combine maximum strength with the minimum of weight and size, and must provide for easy maintenance. Finally, the design must not interfere with rapid access to or escape from the seat.

2. DISADVANTAGES OF THE BUCKET-SHAPED SEAT

The shaped or "ploughman" seat with a perineal elevation (or pummel) has been widely used in the Royal Navy, but it is clearly unsatisfactory in all respects:

i. The subject fits in the seat "like a snail in its shell," and thus for comfort it is imperative that the buttocks should be related correctly to the corresponding concavities of the seat. The size and shape of the buttocks, however, varies considerably from person to person, so that few people can fit comfortably into a seat of one particular size and shape.

ii. The shaped seat results in pressure being fairly evenly distributed over the whole surface of the buttocks. Therefore, the maximum pressure is taken off the skin over the ischial tuberosities and excessive pressure is applied to the surrounding areas. As pointed out previously, anatomical considerations make this undesirable.

iii. It is difficult to change the position of the buttocks even slightly in the alert position, and almost impossible to adopt a position of comfort during periods of relaxation.

iv. The design of the seat makes the presence of drainage-holes in its most dependent part essential to prevent the operator sitting in a pool of water. Such holes and other irregularities of the seat-surface are to be strongly deprecated, for they cause localized areas of skin to be subjected to excessive pressure with resulting discomfort.

v. The perineal elevation is presumably designed to prevent the buttocks slipping forward with the movements of the ship. However, any advantage gained in this respect is more than counterbalanced by the discomfort that may be caused by the effects of prolonged pressure in the perineum. In any case body-stabilization can be better provided by the method of counterpressure between back-rest and foot-rest.

3. DIMENSIONS AND DETAILS OF DESIGN[1]

A. Anthropometric Data

The calculations for the dimensions of the seat are based on an american report. This is used as a standard reference for anthropometric data, because it was available before any british survey and because the method of presentation of the data is particularly suited for use in the problems with which we are concerned. From the point of view of our investigations, comparison of the measurements compiled in the american survey with the body-measurements of british tank-personnel and with our own observations showed no appreciable differences between the selected groups of american and british subjects. On occasions when no relevant data were available, the required measurements were obtained from representative groups of individuals.

B. Vertical Adjustment of Seat

In order to accommodate operators within the 90% range so that the eyes of the operators of varying sitting-heights are in line with the sight, the seat must have a vertical adjustment of 4 inches [10 cm.].

C. Body-Stabilization

For naval purposes, body-stabilization is of prime importance, and it was therefore given first consideration in the design of the seat. As mentioned earlier, body-stabilization is best achieved by counterpressure, and the ideal position for body-stabilization is the one in which the maximum counterpressure can be developed between the feet and the back. The more the position varies from the optimum, the greater the output of energy necessary to maintain equivalent pressures, since the muscles are working at a decreasing mechanical advantage. Previous work on naval problems indicated that the thrust of the legs against a foot-rest rises with the increasing knee-angles, at least up to 135°. A later investigation by Hugh-Jones (1947) went further and showed that (i) when the angle of the thigh to the body remains constant, the maximum thrust rises as the knee-angle increases up to a well-defined "limiting angle" of 165°–170° above which, as the knee straightens and then hyperextends, the thrust obtainable falls precipitously; (ii) with the knee at this angle (165°), the maximum pressure can be obtained when the angle of the thigh is 70°–75° to the body; (iii) the mean maximum instantaneous thrust of 32 service personnel was 691 pounds [313 kg.], and it was concluded that 500 pounds [227 kg.] could be reasonably expected of all persons. These findings support those of Müller (1936). He found that maximum thrust with the legs in a seated subject was obtainable when the seat-surface was at the same height, $\pm$ 4½ inches [12 cm.], as the feet, and the distance from the back of the seat to feet was 2–4 inches [5–10 cm.] shorter than that of the outstretched leg. In the optimum position, one subject exerted a maximum force of 430–450 pounds [195–204 kg.].

It has been demonstrated that, in the range of leg-angles investigated (i.e. thigh to vertical 75°–90° and knee-angle 90°–135°), the pressure that could be maintained without discomfort was an average of 54% of that developed instantaneously. Although it has not been investigated in the optimum position, it is reasonable to suppose that a similar relationship will hold. This fact makes it all the more important that the operator should be in the best possible position for exerting pressure as, although he may be able to obtain in other positions more than the pressure required for instantaneous body-stabilization, he will be less able to maintain it.

As noted above, maximum pressures are obtainable when the thigh is at an angle of 70°–75° to the body-axis. However, the position imposed on the operator would prove uncomfortable if maintained for long periods as, when the thighs are elevated, the pelvis tilts and the weight of the body is transferred from the skin over the ischial tuberosities to

[1] Full details are given in a report by H. D. Darcus (1946) to the Gunnery Sub-Committee of the Royal Naval Personnel Research Committee.

that over the sacrum and gluteal muscles, which is not designed to withstand prolonged pressure. Furthermore, elevation of the thigh would necessitate the seat being sloped correspondingly in order to support it. This is undesirable as it would lead to complications with regard to the adjustment of the eyes to the eyepieces of the binoculars. It was decided that the advantages of increased counterpressure gained by sloping the thighs are outweighed by the complicating factors introduced. Therefore, it was concluded that the ideal position for body-stabilization in ocular sights is with the thighs horizontal and the knee-angle at 165°.

The explanation of the existence of a well-defined limiting angle seems to be due to the fact that, with a man of average bodily dimensions sitting with his legs in such a position, the line of thrust passes through the pivotal axis of the backrest, when the latter is in the optimum position. If the knee-angle is smaller, the thrust is directed above the backrest, so that when exerting pressure with the feet, there is a tendency (which has to be restrained) for the upper part of the body to be pushed back. Conversely, if the knees are held at an angle greater than 165°, the thrust tends to incline the body forward. Both these movements result in instability and loss of counterpressure. Recently, it has been shown (Haxton, 1945) that, in cadavers, the increase of tension resulting from increasing the knee-angle may be due to the patella being drawn upwards over the femoral condyles and thus being displaced further from the centre of the knee-joint as the knee is extended; this allows the quadriceps femoris muscle to work at a greater mechanical advantage.

From the observations outlined above, it will be obvious that it is necessary to have a seat with a foot-rest adjustable so that, in different individuals, a knee-angle of 165° is possible. In practice, an angle of 160° is aimed at, for when counterpressure is applied the knee-angle tends to increase due to " give " in the seat-structure.

Tests have shown, that, when in the optimum position, the stability is so great that a subject can remain in the seat when it is rolled from side to side, even when less than the maximum counterpressure is being exerted. In naval warfare, it has been estimated that the maximum extrinsic force tending to displace an operator from his seat is about 200 pounds [90 kg.], whereas the mean pressure that can be maintained with each leg in the position described is about 500 pounds [227 kg.]. Care should be taken that the mechanical design of the seat is sufficiently robust to withstand these pressures without undue " give " or fracture.

D. Seat-Cushion

i. *Dimensions.* Reference to anthropometric data shows that the minimum satisfactory width of the seat-cushion is 15 inches [38 cm.]. The antero-posterior depth of the cushion has to be limited to the length of the underside of the thigh of the smallest individual in the 90% range, in order to prevent interference with the movement of the legs and to prevent pressure on the back of the knee. From this consideration, it is recommended that the depth of the seat should be 18 inches [46 cm.]. It was found, however, that a seat-cushion of these dimensions was not wholly satisfactory, for when the subject is sitting with the upper surfaces of the thighs horizontal and the knee-angle at 160°, the distal part of the underside of the thighs is left unsupported by the cushion, because the underside of the thigh slopes upwards at an angle of about 10° to the horizontal in the average subject. To allow for this and, at the same time, to retain the advantages of a flat seat, the front 8 inches [20 cm.] of the cushion should be sloped to an angle of 10° to the horizontal and the back 10 inches [25 cm.] disposed horizontally.

ii. *Resilience.* As a result of comparative tests, we have found that the most suitable method of padding the seat-cushion to obtain the required resilience without lateral or antero-posterior sway consists of tempered-steel strips fixed to a steel base-plate. This method has the added advantages that the steel strips can be made to give any required degree of resilience and that they are extremely durable. Moreover, the resilience does not vary even with prolonged use. Being metal, the springs are fire- and mould-proof. Rust can be combated by cadmium-plating.

The springs should be fixed transversely as, no matter where the buttocks of the operator are placed in an antero-posterior direction, the degree of resilience will then be the same. The risk of sitting on the insertion of the spring, where there is little or no resilience, or of pressure from this part of the cushion on the underside of the thighs, is also avoided.

It is important that the front part of the cushion should be rounded and softly sprung to prevent undue pressure on the underside of the thighs, and also to allow for any variation in the slope of the underside of the thighs in different individuals.

iii. *Seat-covering.* Tests have shown that the most successful seat-covering is first-quality tropicalized hide or certain polyvinyl chloride leather-cloths, both of which fulfil all the requirements for naval use. The seat-covering should be fluted transversely. This allows the covering to be slack, so that no undue strain occurs when the cushion is compressed. Furthermore, the shallow furrows between the flutes permit air to circulate between the cushion and the buttocks of the operator. They also provide channels along which water can drain from the surface of the cushion. The flutes are transverse to avoid uncomfortable pressure into the natal cleft. A layer of DDT-impregnated rubberized horsehair stitched to hessian is interposed between the seat-covering and the springs to act as a " buffer ". Incidentally, it adds to the resilience of the cushion. The horsehair is sewn into the flutes to prevent it from moving with use.

E. Foot-Rest

The position of the foot-rest in relation to the seat was determined by reference to the optimum position of the legs for body-stabilization. In order to allow subjects within the 90% range to sit with their legs in the correct position, the foot-rest must be adjustable. Fortunately, there is a good correlation between the leg-length and sitting-height, so that a link-mechanism can be used which permits simultaneous adjustment of the seat-to-ocular-height and seat-to-foot-rest lengths by moving a single lever. For the largest man in the 90% range, the lowest part of the foot-rest should be 8 inches [20 cm.] below the level of the compressed seat-cushion and 47¼ inches [120 cm.] from the back of the seat and, for the smallest man in this range, the lowest part of the foot-rest should be 7 inches [18 cm.] below the level of the compressed cushion and 41 inches [104 cm.] from the back of the seat. The

slope of the foot-rest should be at right-angles to the leg-bones, and as the leg is held at 20° to the horizontal in the optimum position, the foot-rest should slope at 110° to the horizontal. The length of the foot-rest should be 14 inches [35.5 cm.] and the width 15 inches [38 cm.]. A heel-rest must be fitted to the lower end of the foot-rest. It should project at right-angles to the foot-rest and be at least 3 inches [8 cm.] deep in order to give efficient and comfortable support to the heel.

F. Back-Rest

i. *Dimensions.* As mentioned under the requirements, the back-rest should be placed so that it corresponds to the maximum concavity of the lumbar curvature. The height of maximum concavity of the lumbar curvature above the ischial tuberosities was determined, and, in individuals within the 90% range of sitting-height, it was found to vary between 8 inches [20 cm.] and 12 inches [30 cm.]. It was thought at first that a back-rest of adjustable height would be necessary in order to give sufficient support to the back of all individuals (Hebestreit, 1930), but practical tests showed that a back-rest 5 inches [13 cm.] in vertical depth, which is almost the same as that recommended by Hebestreit (1930), and with its centre 10½ inches [27 cm.] above the compressed seat-cushion is satisfactory. A back-rest of this width is sufficient to support the pelvis directly, which is important if maximum pressure against a foot-rest is desired (Müller, 1936). If the pelvis is not supported the back-muscles are liable to undergo considerable strain to keep the pelvis in position, and the maximum pressure is decreased. The back-rest should be placed ½ inch [1.27 cm.] behind the back edge of the seat in order to allow for a good sitting-position for the operator. The curve of the back-rest should correspond to the natural curvature of the lumbar region as accurately as possible. The average curve, 10 inches [26 cm.] above the level of the seat in subjects sitting erect, was found to be the arc of a circle of radius 7$^{5}/_{16}$ inches [18.5 cm.]. The width of the back-rest should be 15 inches [38 cm.].

ii. *Pivot.* It has been estimated, from the fact that the force exerted against the back-rest by counterpressure from the feet is considerably greater than that derived from the weight of the trunk, that the pivot should be placed a certain distance below the level of the back-rest. A satisfactory position was found to be 1 inch [2.54 cm.] below the centre of the back-rest.

iii. *Padding.* It is recommended that the back-rest should be padded similarly to the seat-cushion. It should consist of four horizontal ½ inch [1.27 cm.] tempered-steel-strip springs fixed to a correctly curved steel-plate. If the springs are disposed vertically, hard upper and lower borders will result. The curved steel-plate must be strong enough to prevent bowing. The springs should be covered with first-quality tropicalized hide or polyvinyl chloride leather-cloth with rubberized horsehair interposed between the covering and the springs. The borders of the back-rest should be widely curved and the corners should be curved from above downwards as well as from before backwards, thus forming quadrants of a sphere, the radius of which should be about 2 inches [5 cm.].

The supporting frame of the back-rest should be collapsible in order to facilitate entry to the seat, when necessary, from the rear.

G. Lateral Thigh-Support

It was found during the course of investigation on the anatomical seat that the comfort of the operator is increased considerably by the attachment of lateral thigh-supports to the distal part of the sides of the seat. They prevent too great a degree of passive lateral rotation and abduction of the thigh, which tends to occur in this position, and so obviate strain on the muscles of the inner side of the thigh (the adductor and medial rotator muscles) which must otherwise remain in a state of permanent tonic contraction in order to resist this movement. The muscular activity thus necessitated in the absence of these supports is liable to lead to fatigue. They can help to aid body-stabilization to some extent if the thighs are forced against them, and they will also assist in preventing the operator being thrown from his seat with an unexpected movement of the ship. Furthermore, the supports can be so placed that controls attached to them are in the correct position for precise manipulation by the hands. The inner surface of the supports should be flat and the edges rounded. No padding is necessary, as the pressure against the supports will neither be of great magnitude nor prolonged, but they should be covered with heat-insulating material.

It is suggested that these supports should be fitted whenever practicable, but they can be removed in circumstances in which they are liable to interfere with the manning or leaving of the seat.

4. ADJUSTMENT OF THE SEAT

In order to derive full benefit from good seating, it is absolutely essential that the operator must be able to adjust himself rapidly and accurately to the seat. The adjustable seat can be made completely satisfactory provided that there is sufficient supervision to make sure that each seat is in fact kept properly adjusted to the needs of the individual. It is recommended that this should be the specific duty of one particular officer. All operators should at some convenient time be fitted to the seat by the responsible officer, and each should be given the number or letter of his seat-adjustment, so that when he has to take up his position in the seat he can immediately adjust it correctly (fig. 2).

It is obvious that, although in general there is a good correlation between sitting-height and leg-length, this is not absolute. A further variable that has to be borne in mind, and which is liable to alter the correlation, is the variation in the thickness of the soles of the different types of footwear worn under operational conditions. Therefore, not all subjects will be able to sit in the optimum position, and the seat-adjustment of some will have to be determined intelligently. For example, the correlation of leg-length with sitting-height may vary, even in the 90% range. Since it is essential in all cases to relate the eyes correctly to the binoculars, in some subjects it may be impossible at the same time to achieve the optimum position of the legs.

5. CONCLUSION

This paper describes the desiderata for, and the design of, an adjustable seat for use in naval war-weapons. Although this seat was specifically designed for use with sighting-apparatus, the principle of maintaining stability by the use of counterpressure between the feet and the back-rest is so important that similar seats are to be tried experimentally in other situations aboard ship. It may also be pointed

Continued at foot of page 37

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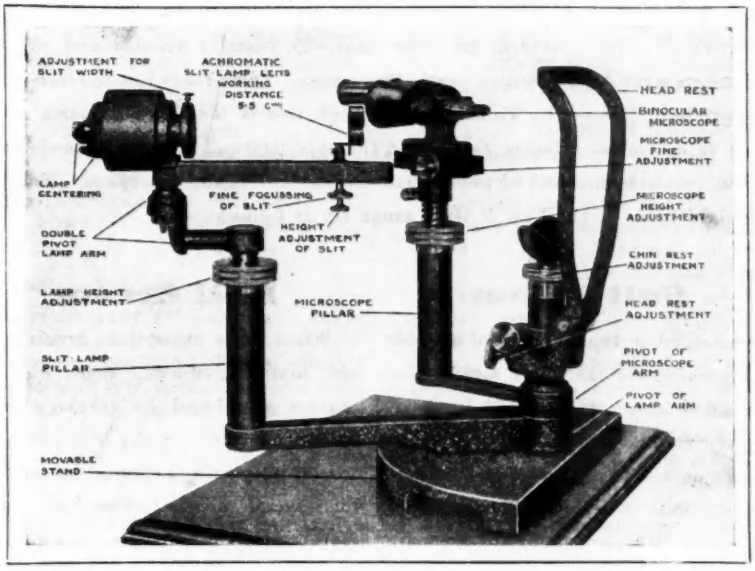

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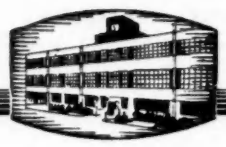

PERSONNEL SELECTION IN THE ROYAL NAVY

ALEC RODGER M.A.

Senior Psychologist to the Admiralty

Almost exactly six years ago the Admiralty decided to overhaul the procedures adopted in selecting new recruits for the Navy and in allocating them to their various naval employments. They asked the National Institute of Industrial Psychology to take part in a preliminary survey, and I was fortunate enough to be detailed for the task. A committee of three—Dr. Desmond Curran (the Navy's consultant in psychological medicine), an executive officer, and myself—toured the country for several weeks, collecting evidence about the nature and efficiency of the existing methods of selection and allocation. We returned to the Admiralty loaded with information and ideas, which we fashioned into two schemes for immediate application. One scheme was designed to improve the existing selection procedure in Combined Recruiting Centres; the other was intended to improve the allocation procedures used in the Navy's Entry Establishments.

Scheme for Combined Recruiting Centres

The routine procedure of the Combined Recruiting Centre we had found to be of a fairly primitive kind. The recruiters were mostly pensioner chief-petty-officers and petty-officers, and their job was to interview very briefly men who had chosen service with the Navy. At the end of each interview they had to decide whether the candidate should be accepted or rejected. In the case of the accepted men, they had to go further by designating each one for a particular branch of the Navy.

It seemed clear from our survey that this plan was faulty, especially because it was admitting men of low intelligence and men of low stability. What was needed primarily, we felt, was a more thorough survey of each candidate's past record before a decision was made about him. So the Admiralty agreed to provide the pensioner-recruiters with recruiting assistants. They agreed, moreover, that these recruiting assistants should be well-chosen personnel from the Women's Royal Naval Service (Wrens). The Wrens were to be selected and trained for the purpose and were to be supervised, in their recruiting centres, by three peripatetic psychiatric social-workers. They and their supervisors were to be members of the staff of the newly-formed department of the Senior Psychologist at the Admiralty. It had been agreed that the Senior Psychologist himself should be directly responsible to the Second Sea Lord, the Chief of Naval Personnel.

The Wrens went to their recruiting centres in pairs with a four-point programme. First, to get each candidate for the Navy to complete a simple biographical questionnaire; secondly, to give him a paper-and-pencil intelligence test of the non-verbal type; thirdly, to give him a colour-vision test of the Ishihara type; and fourthly, to interview him. The object of this procedure was to collect relevant data about each man before the recruiter saw him at all. It enabled the recruiter to start his own interview with a solid foundation of fact about each candidate's qualifications.

Scheme for Entry Establishments

The second scheme produced changes in the routines adopted in Entry Establishments in allocating accepted men to their particular employments. There were, at that time, six or seven large establishments receiving up to about 500 men a week each. For example, one establishment dealt with men who had been selected by recruiters for the air-mechanic branch of the Fleet Air Arm. Its function was twofold: first, to allocate all its entries to the electrical, engine, airframe and ordnance categories; and secondly, to detach the most promising of the men in each category for higher-grade training which would raise them from the mechanic group to the status of fitters.

In this particular establishment, the new routine worked in this way. On the day after entry, a batch of new recruits had what was called an " information hour," in which three people gave twenty-minute talks. First came the Training Commander, who welcomed them to the Navy and spoke simply and effectively about its traditions of comradeship, gallantry and discipline. The schoolmaster talked to them about the importance of mathematics to all air-mechanics and, in humorous vein, encouraged them to tackle the subject seriously. Last came the resident civilian-psycholo-

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ANATOMICAL PRINCIPLES IN DESIGN OF SEATS

Continued from page 36

out that many of the other principles of seating elucidated in this investigation may be directly applied to the design of seats for industrial purposes. It is important, however, to realize that the final design of a seat in any particular industrial situation must be considered as an individual problem, owing to the diverse character of the factors involved.

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gist, or his senior personnel-selection officer (P.S.O.). The aim of their contribution was to outline the duties and training-programme appropriate to each of the categories available, and to say something about the regulations for pay and advancement. By judicious emphasis on one factor or another, an attempt was made to ensure that the preferences later to be expressed by the men agreed reasonably well with the current "quotas" laid down by the Director of Manning. For example, there was always likely to be an excess of candidates for the "engine" categories, so it was regarded as permissible for the P.S.O. to draw attention to the fact that this was a rather dirtier kind of job than the others.

The "information hour", then, constituted the first stage of the new allocation-procedure for use in Entry Establishments. It was regarded as being of considerable importance, because it was believed that, given accurate and relevant information, the men would themselves be stimulated to do a little self-selection for their naval employments.

The second stage consisted of some standard written tests for intelligence, mathematical attainment and mechanical aptitude. We seldom made use of practical manipulative tests, because for ordinary purposes of selection few of them are really worth the time they take.

The third stage of the Entry Establishment procedure consisted of about 22 hours' schooling in mathematics provided by the schoolmaster. It began with an examination and finished with a parallel examination designed to show what progress had been made by each man during his short course of instruction.

The fourth stage, which came some five weeks after the recruit's entry, was his interview with a P.S.O. The main aim here was to discover what ideas each man had formed about his suitability for the various categories available and to consider them in the light of his qualifications as revealed by the interview and by the data provided by the tests he had taken earlier.

The fifth stage was the "categorization conference," at which—under the chairmanship of the Training Commander—the P.S.O., the schoolmaster and the divisional officer (company commander) concerned discussed each man and arrived at a decision about his allocation. Sixth and last came the promulgation of the decisions. This was done in a rather formal manner, at a meeting deliberately planned to be reminiscent of a prize-giving. The announcements were made by the divisional officer concerned. But he omitted the names of men who had not been allocated to any of the categories for which they had expressed a preference. These men were told to stay behind. Each of them was given a private and sympathetic explanation of the decision reached by the categorization conference and was told that he could make an appeal on the following day if he wished to do so.

Results of the Schemes

Afterwards, the men went from the establishment to other places for their specialized training. Careful follow-up was done, and it was later found that the introduction of the new allocation-procedure had apparently produced a substantial reduction in the over-all failure-rate in technical courses. Formerly the failure-rate had been 14·7%; now it was exactly 4·7%. A financial calculation by an independent assessor indicated that the saving in the air-mechanic and air-fitter groups alone amounted, in a twelve-month period, to about £100,000. The number of cases on which this estimate was based was no small sample; the enquiry covered 16,500 men.

So much for the Navy's Combined Recruiting Centre and Entry Establishment schemes. The former has been applied, so far, to over 950,000 men (including, of course, men rejected as unsuitable for the Navy). The latter has been applied to about 400,000 men; that is, to over half the wartime Navy.

Procedure for Officer-Selection

Finally, I must make some reference to the development of new officer-selection procedures. Here we proceeded more slowly, for several good reasons. Our first task was to discover experimentally whether an ordinary written intelligence-test would help in the elimination of intellectually-unsuitable candidates. We did this by giving a standard test to about 500 cadets at the very start of their officer-training, and by locking up the papers until they had all had a chance to be promoted to commissioned rank. Then a comparison was made between their intelligence-test results and their passing-out marks. The agreement was found to be high, and it was clear that if the results of the test had been disclosed, and had been used in the sifting of the cadets, most of the potential failures could have been eliminated at the cost of only a very small proportion of the men who actually managed to gain promotion.

Having demonstrated the value of an intelligence-test for this purpose, we went on to demonstrate the value of an industrial psychologist's interview. Another 500 men took part in this experiment. Each was interviewed for fifteen or twenty minutes by a psychologist, and a short written report was prepared immediately. Later follow-up indicated that the board's assessments proved justified in 61% of the cases; the industrial psychologist's score was 71%. The conclusion reached from a detailed study of the data was that an ordinary selection board aided by reports from a psychologist could probably make appreciably better predictions than either of them could make independently.

These two investigations—into the value of an intelligence test and an industrial psychologist's interview—led to the general adoption of these two techniques and to still further developments. A modification of the War Office Selection Board method was introduced, and has since been applied to over 10,000 candidates for temporary commissions in the Navy. There are two major differences between the War Office and the Admiralty arrangements. First, the Admiralty's procedure is normally spread over a three-month preliminary training period, instead of being concentrated into two or three days. In this way the Navy is able to take into account impressions formed by training officers over a long period. Secondly, the Admiralty Selection Boards have no psychiatrists or educational psychologists on them. All the psychological testing and interviewing is done by an industrial psychologist.

Let me add in conclusion that when the Senior Psychologist's Department at the Admiralty was founded in 1941 it was agreed that it should be concerned not only with personnel-selection problems but also with other psychological matters. It deals, for example, with training and examination procedures, with documentation, with methods of work and with the improvement of working-conditions. This we arranged quite deliberately. Our pre-war experience in the field of industrial psychology had led us to the conclusion that it would be unfortunate if we were forced to attend to only one side of the task of fitting the new sailor to his wartime job.

PSYCHOLOGICAL PROBLEMS IN FLYING PERSONNEL

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1 Methods of psychological selection
2 Role of the psychiatrist
3 The " Harrogate Experiment "
4 Research in Bomber Squadrons
5 Fear
6 Limiting operational duties
7 Endogenous factors

When considering the problem of the psychological management of aircrews, it is important to realize what a big problem this was in the war which has just ended. It was not big simply because of the numbers of men involved, but also because of the disastrous consequences of the continued inefficiency of one member of an aeroplane's crew. When a man had been fully trained, he was in action against the enemy for a comparatively short time—for a maximum of about 30 trips in a bomber-tour of duty, or 200 hours in a fighter. During the major part of this time in the air he was not actually engaging the enemy, and indeed reconnaissance in Germany showed that quite a small proportion of the bombs dropped found an important target. Only when all the members of a crew were highly efficient, and were also successful, was the return worthy of the fortitude needed to complete a tour of operations, whether this was carried out in bombers, fighters, or reconnaissance.

But another aspect of this balance must be considered—the economic aspect, which sets against the damage done to the enemy all the time of instructors, ground-staff and aircraft, in training a man and in keeping him in the air, and all the manpower needed to design, build and maintain the aircraft which he uses. When this is considered, it is seen that the airman stands at the apex of a very wide pyramid, and that the waste incurred by the inefficiency of a member of a crew who vitiates the result of a single trip must be measured upon this basis. This crucial man, the airman, worked in an environment of physiological and psychological stress which was bound in time to reduce his efficiency, and his welfare presented problems of the first importance which were probably unique in the fighting services.

Psychological problems existed in all stages of training in aircrew of the Royal Air Force, as well as in all the operational commands, and of course the problems differed with the nature of the duties. The study of these problems, and the application of the results which were obtained from these studies, was continued throughout the war, in the fields of selection, prevention of inefficiency and neurosis in aircrew under training and in operational duties, and the treatment and rehabilitation of those who broke down. Collected *Reports of investigations into psychological disorders in flying personnel during the war 1939 to 1945*[1] have recently been published by His Majesty's Stationery Office as Air Ministry Publication 3139. These reports contain much detailed information on many aspects of the subject which cannot be included in this short paper.

The management of psychological problems differed in detail in different forms of flying duties, so that I shall confine myself to one of these, and have chosen bombing. There are several reasons for this choice. In Bomber Command the problem was a large one—one third of all cases of neurosis in aircrew in the RAF occurred in Bomber Command, while very few men completed an operational tour in heavy bombers as completely fit men. They nearly all lost weight, had terror-dreams, or became jumpy and depressed. A very wise station-commander said that few of his men took their tour of night-bombing in their stride, and most of those who completed their tour only just managed to do so. Over 50,000 men lost their lives in bombing operations and only a minority of those beginning succeeded in completing their full operational tour of duty. Nevertheless, in this Command the issue was a simple one, for it involved the ability of a man to withstand persistent and repeated fear; other factors, such as fatigue or physical changes in environment played little part in the production of inefficiency or neurosis.

By the time a man had reached Bomber Command, selection had been undertaken, and the major problem was that of prevention of neurosis, for it was found that if, when a man had broken down under the stress of his duties, he required more than the most superficial psychotherapy, he was unlikely to return to flying-duty and to remain efficient.

1. Methods of Psychological Selection

Research into the most profitable methods of selection was undertaken throughout the war by the Training Research Unit and by the team of psychologists working under Professor Bartlett in Cambridge. Research had necessarily to follow two lines of enquiry, the first to determine aptitude for flying itself, and the second to distinguish the characteristics which safeguarded a man against the fears and stresses of operational flying. The first exercised the industry of a large group of workers, particularly in the United States, and it involved the construction and validation of aptitude-tests, some of them simple questions and answers, others complicated performance-tests such as the experimental cockpit used in Cambridge. As a generalization it is true that the more closely the test-situation resembled that within the aircraft, the greater was its reliability. Reid has recently shown in a follow-up of men who had reached night-bombing operations that there was a close correlation between performance in the Cambridge cockpit and efficiency in bombing operations, although a similar correlation of other tests was insignificant. A detailed description of the methods of selection which were devised, rejected, modified, applied and validated is far beyond the scope of the present short paper.

In the RAF initial selection was carried out by two parallel boards, one medical and the other executive, composed of senior officers who had flown. These boards

[1] Published by H.M. Stationery Office, London, 1946.

rejected those grossly unsuitable through physical shortcomings or ineptitude. It was during flying-training that the main selection occurred. At all stages the unsuitable were eliminated in the aptitude-testing which took place in the training aircraft, and flying-instructors—who often had considerable aptitude for the recognition of unsuitability—were instructed in the methods of selection. There was naturally a reluctance to lower the percentage of men passed out from any particular course, but, as the war progressed, instructors learnt that it was more profitable to reject the backward than to push them through. There was also the difficulty, which instructors in Flying Training Command sometimes had, of lack of personal knowledge of the conditions in operational flying. This prevented recognition of those personality-defects which militate against a successful career in operational flying.

A considerable advance occurred in the selection of bomber crews, when grading schools were instituted. In these schools all flying pupils flew under training in Tiger Moth planes for 12 hours. They were then graded on a system of marks which evaluated most aspects of the man's performance, and were selected for flying-duties as pilot, navigator or bomb-aimer. Late in the war, a much more elaborate system of vocational selection for the different aircrew duties was devised and put into operation, but as the time from the commencement of training to the end of a night-bomber tour was often over two years, the final validation of this system is not yet available.

2. Role of the Psychiatrist

Psychiatric selection—the examination by trained psychiatrists for evidences of handicapping personality-traits, and expert assessment of the personality—was not practised as a routine. There were several potent reasons for this. The first was a natural suspicion which the executive flying officers had towards doctors in general and psychiatrists in particular—a suspicion which gradually became less as the war went on. Then there was a quite justifiable feeling among flying personnel, that they were the best judges of the kind of men that they would trust in an aircraft. Lastly, there was the very material reason that the constant need for men was so great that no scheme of selection was admissible if it brought about the rejection of a significant proportion of the potentially successful for the sake of eliminating a small number of potential failures.

It was, therefore, incumbent upon the psychiatrists to prove that the results of their methods of personality-selection warranted their adoption. This was done, but again the time required for validation prevented any attempt to institute the methods in the machinery of routine selection. Psychiatric selection did occur, however, for, as had been mentioned already, not only were the unsuitable weeded out *ab initio* by selection-boards, sometimes with reference to psychiatrists, but re-selection boards employed a psychiatrist. During the months and years of training, selection continued, the doubtful or the neurotic being referred to the psychiatrist. In the later stages of training, when men were flying heavy bombers, the conditions began to approach those of operational flying, so that the natural selection which occurred was at that stage based upon personal aptitude for operational duties rather than for flying itself.

3. The "Harrogate Experiment"

The "Harrogate Experiment" was a large-scale attempt to validate methods of psychological and psychiatric testing against performance on night-bombing operations. This experiment was devised on the psychological side by Professor Bartlett and on the psychiatric by Sir Charles Symonds, who used a method of scoring personality-traits based on the observations of R. D. Gillespie. The experiment was to take 1,000 men who had already been selected for flying-training, and who had completed their elementary flying-training, and subject them to an hour's psychiatric interview. This interview was carried out on 500 men each by two trained psychiatrists. They scored the presence of 10 personality-traits which had been found by Gillespie to occur in neurotic flying personnel, and made an independent psychiatric assessment, in four grades, upon the basis of the whole interview. The traits incriminated were:

1. A family history of psychiatric disorder
2. A previous personal nervous breakdown
3. Evidence of morbid fears and anxiety
4. Physiological instability, shown by such changes as fainting
5. Timidity
6. Lack of aggressiveness
7. Lack of persistence
8. Affective lability
9. Obsessional features, i.e., psychological immaturity.

The assessment of predisposition to neurosis was independently rated as none, slight, moderate, or severe.

The traits which related most closely to the psychiatric assessment of severe predisposition were: previous nervous breakdown, timidity, lack of aggression or of persistence, affective lability, and psychological immaturity. It was concluded that a method of elimination on the basis of assessment of predisposition might be practicable and profitable, but it would be neither practicable nor desirable to replace the psychiatric assessment by a trait-score. Subsequently, some of the tested men were followed through operational flying, and it was found that these conclusions were substantiated, but it was also found that the success of the method depended upon the personal flair of the psychiatrist for this work. Some details of the method are available in the collected reports already quoted.

4. Research in Bomber Squadrons

When a man had reached a squadron, the problem was then to maintain his efficiency in spite of the dangers and stresses to which he was subjected. The executive officers were mainly responsible for handling this problem, but as the war progressed they tended to call for psychiatric help. The necessity for such help was shown by the high rate of breakdown among aircrew engaged on operations. In the year 1942-43, 2,503 cases of neurosis in flying personnel were handled by neuro-psychiatrists, and 942 of these came from Bomber Command alone. Because of the necessity of recording the occurrence of neurosis in aircrew in different duties and circumstances, a central Registry was set up by the Consultant in neurology, Sir Charles Symonds. To this Registry each neuropsychiatric specialist made a card-return for every member of an aircrew referred to him with

symptoms of a psychological disorder. The card contained fairly comprehensive data about the man's flying career, including his squadron, type of aircraft flown, duties, total flying-hours, and operational flying-hours, as well as an account of his illness, with a brief résumé of the main causal factors connected and unconnected with flying, and the treatment and disposal recommended. All the data were immediately transferred to a punch-card system, so that it was possible to review contemporary events in this field with some accuracy. In this way conjecture was reduced to a minimum, and advice upon the management of aircrew could be based upon facts. The information obtained in this way led to a statistical survey of the situation in all commands, flying-duties, and squadrons in the RAF. This was reinforced by careful clinical studies of special problems as they arose, and by clinical examination of groups of subjects representative of the whole group under survey. Some of the reports which were based upon this work are reproduced *in toto* in Air Ministry Publication 3139, already quoted.

Another method of study of the causes of inefficiency and neurosis in aircrew was that of personal field-surveys in the squadrons. In this work Sir Charles Symonds and I independently visited representative squadrons for each of the flying-duties undertaken in the RAF, and canvassed the opinions of commanding officers of stations, squadrons and flights, as well as of the medical officer, upon such subjects as the early signs of inefficiency and neurosis in flying personnel, the factors which they considered to be important in causing this inefficiency, and the methods which they thought should be adopted to reduce the incidence of neurosis.

Some of the information obtained from the card-return is illuminating. The incidence of neurosis in different duties showed wide differences, as is revealed in the ratios (table I), expressed as an approximate percentage of average numbers of personnel for the year 1943:

TABLE I. PERCENTAGE INCIDENCE OF NEUROSIS FOR DIFFERENT DUTIES

Night-bomber	12
Day-bomber	11
Day-fighter	6
Night-fighter	4
Coastal reconnaissance ...	3½
Training command	1

This table shows that there was a close relationship between the hazard of the duty and the incidence of neurosis arising in it. It shows that the incidence was 12 times as high in night-bomber squadrons as in Flying Training Command, although the number of psychologically-unsuitable men was, by natural selection, very much lower in the operational than in the training units, which underlines the part played by hazard in the etiology of the neurosis. In this respect it is interesting that the incidence in night-bombing squadrons was twice that in day-fighter squadrons.

In Bomber Command, which was responsible throughout the war for one-third of cases of neurosis in flying personnel in the whole RAF at home and overseas, the incidence of neurosis in operational squadrons was about four times that of the whole service, over twice that in Fighter Command, and three times that in Coastal Command, while it was over 10 times that in Flying Training Command. Furthermore, the incidence in operational squadrons in each command was many times higher than in training units within the command.

It was clear that the most potent factor in causing neurosis in aircrews was fear. All other contributory factors added to the stress which the man had to withstand, but in the great majority of cases they were unimportant. The hazard of the duty, reflected in the wastage-rate in the squadron, was found to be directly and closely related to the incidence of neurosis. This is shown in table II.

TABLE II. RELATION OF NEUROSIS-INCIDENCE TO WASTAGE-RATE

Duty	Relative incidence of neurosis	Relative flying-hours per casualty in these duties
Night-bombing	12·0	160
Day-fighting	6·0	188
Night-fighting	3·4	231
Coastal reconnaissance...	3·3	360
Training	1·1	1,960

Fatigue was found to be of etiological importance in very few cases of neurosis, and physical causes apart from illness and injury were rarely considered contributory. This was at variance with views that were held early in the war, and in Germany throughout it. It had been supposed that anoxia, altitude, or vibration and noise caused changes in flying personnel which predisposed them to psychological disorder. That the psychiatrists failed to recognize any such factors is shown in table III.

TABLE III. NEUROSES CAUSED BY FLYING-DUTIES

Recognized Causes	Number of cases (Total 2,200)	Percentage of Causes	Cases
Psychological (fear, etc.) ...	2,191	76	99·6
Physical injury	399	14	18·1
Physical illness	212	7	9·2
Air sickness	52	2	2·4
Exhaustion	43	1	2·0
Cold	0	0	0
Altitude	0	0	0
More than one cause ...	676	23	—

It will be seen that in virtually every case of neurosis there were psychological causes recognized as playing a major part in the etiology of neurosis in aircrew, while in 2,200 cases physical factors specially encountered in aircraft—cold, anoxia, altitude—were never thought to have played any significant part.

5. Fear

The field-survey in the squadrons led to the same conclusions as the statistical survey—that the most potent cause of inefficiency and breakdown in aircrew was fear. Strenuous attempts were therefore made to limit fear, in its intensity, its duration, and its repetition, and to modify the circumstances in which it arose. Many lines of approach were open, and as many as possible were used. First, there was the attempt to encourage the development of fortifying factors in the men exposed to fear. This entailed encouragement of the right kind of leadership in the flight- and squadron-commander's development of group-spirit in the station, particularly in respect to the

maintenance of high confidence of the aircrews for their ground-crews, for their aircraft, and for their leaders. It also involved attention to the mode of living of the aircrews, encouragement of physical fitness and of an orderly method of living, as well as the limitation of fatigue. The views of experienced commanders upon the importance of these things have been given in the collected reports in Air Ministry Publication 3139.

Secondly, every effort was made by the executive to limit the fear-provoking situations as far as was possible. It was of course impossible to limit the hazard of operational flying which resulted from enemy action, and navigational and technical aids to the aircrew were pushed to a high degree of perfection, with the object of reducing the hazards of flying in all weathers at night. But when all this was done the danger was still very great, the fear to which it gave rise was often intense, and once the aircraft was airborne, limitation of the effects of this fear lay in the group-spirit of the crew, the leadership of the captain, and the previous training and background and personality of the individuals.

It was possible to reduce the anticipatory fear that came before the operational flight in several ways. The crews were informed of details of the flight and target shortly before starting, and after they had had a meal. The time of waiting in the aircraft and on the ground was reduced as far as possible, and cancellation of sorties, which was sometimes unavoidable, was reduced to a minimum. The consultants in neuro-psychiatry visited commands and stations, and there was an increasing realization of the importance of studying the ways of safeguarding aircrew from the stress of the hazard of their duties.

6. Limiting Operational Duties

Besides reducing the anticipatory fear of operational flying, the actual duration and intensity of the fearful period was controlled by the executive. A limit to the number of operational sorties expected of each man was laid down —a limit within the reach of the average and known to the crews. This operational limit was modified from time to time according to the nature and circumstances of the operational flying. It was short when danger was intense, and long and tedious in the routine duties of reconnaissance. Each member of aircrew was expected to complete two operational tours, and he was given a period of alternative flying-duty—usually that of instructing at an operational training unit, between these tours. Any competitive element was eliminated by refusal to recognize voluntary continuation of a tour of duty or return to a third tour of duty except in exceptional circumstances. Although there was a fixed upper limit to the operational duty expected of any one man, the squadron-commander was encouraged to terminate any man's tour before that limit was reached, if he was satisfied that that man's reasonable and efficient contribution to the operational effort had been made. In this way the psychologically less robust were safeguarded, and their efficiency was preserved for their second tour of duty.

The beneficial effect of the operational limit, which was known to the crews, was great. The men knew what was expected of them, they saw a reasonable hope of survival, and they recognized a reasonable equity of sacrifice. The safe and honourable completion of a tour was, more than dramatic achievement or the award of decorations, the hope and aim of all but the exceptional, and its announcement was cause for relief and congratulation, invariably shared by the whole squadron.

The intensity of the hazard within the tour was reduced by spacing the number of operational sorties for any one crew, and by resting a crew after a series of sorties with deep penetration into enemy territory, and to heavily-defended targets.

Finally, the effects of fear were reduced by frequent short leave-periods, known beforehand and almost inviolate, which were spaced throughout the tour; by active programmes of entertainment and recreation; and by creating a communal life within the squadron, all members of which lived in the same mess, with their wives and families living remote from the station.

7. Endogenous Factors

It is not possible to discuss all the domestic and personal factors which contributed to psychological disorders in aircrew, for they were as diverse as in civilian life. In some cases they were the major factor in etiology, but in most they simply contributed a background to the stress of operational flying.

Although every effort was made to reduce the exogenous causes of neurosis in flying personnel, it was clear that the endogenous factors were the more potent. Mention has already been made of the predisposition to break down under the stress of flying. In a psychiatric interview this predisposition was assessed, and by common usage was expressed in three grades—no evidence of predisposition (nil), evidence of predisposition (mild), and predisposition of such severity that it would have led the psychiatrist to reject that man for flying-duties had he seen him on entry (severe). In 2,200 cases of neurosis in flying personnel, in which the psychiatrist considered the neurosis to have arisen as a result of flying-duties, evidence of predisposition to neurosis was found in three-quarters of the total, and of severe predisposition in one-fifth. This contrasted with 3% who were severely predisposed and 12% who were mildly predisposed among normal aircrew.

There was fairly close agreement among psychiatrists in their assessment of the degree of predisposition and in the importance which they gave to it. There was a marked reciprocal relationship between the amount of hazard which a man experienced before he broke down, and the degree of predisposition to neurosis which was recognized in him after breakdown. This relationship is shown in table IV.

TABLE IV. RELATION OF FLYING-EXPERIENCE AND PREDISPOSITION TO NEUROSIS

Flying-experience	Number of cases	Predisposition to neurosis (%)	
		Nil	Severe
No flying	106	14	36
No operational flying ...	676	20	27
Under 100 hours' operational flying	688	26	18
Over 100 hours' operational flying	730	37	11

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PSYCHOMOTOR EFFECTS OF ANALEPTICS AND THEIR RELATION TO "FATIGUE" PHENOMENA IN AIRCREW

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In some experimental subjects a dose of 15 mg. amphetamine may produce striking changes in the performance of psychomotor tests. In several of the tests by which we try to measure the effects of such drugs as amphetamine, both the speed and the accuracy of the performance may vary. Amphetamine produces an increase in speed with some, but not a proportionate increase in errors. In tests in which speed does not vary, like the pursuit-meter, errors may be reduced in number. When subjects are kept awake all night, a deterioration of the performance both in speed and accuracy may be observed during the night and the following day. Amphetamine may partially restore the performance. With a dose of 15 mg., subjects may feel more alert than usual and ready for anything. They may become mildly elated and confident, without the doubts and anxieties and the discomfort of the tension usually experienced before starting a test. On the other hand, tests which without amphetamine are regarded as boring may engage their interest and become absorbing. They may feel able to concentrate on them without the usual diversion of their attention by extraneous events. Attention may seem to be narrowed and focussed upon the task in hand. If they have been deprived of sleep, amphetamine may remove the desire for sleep and the associated feelings of heaviness and listlessness.

It is probable that the improvement in the performance of tests with amphetamine is related to the greater interest which subjects take in them and not to any increase in capacity, since similar improvement may be produced by other means which increase interest. For instance, a similar reduction of errors in a pursuit-meter test may be obtained by causing the subjects to regard a trial as of more than normal importance, or by providing special incentives. In tests in which speed and accuracy may vary, these measures have a less-uniform effect than amphetamine, since they may make a subject either more careful or more rapid in his work, whereas amphetamine nearly always causes an increase in speed and not in accuracy.

Disadvantages of Analeptics

This account suggests that the effects of amphetamine are highly desirable, but there are several sources of danger, which make it unwise to use amphetamine except in special circumstances and with safeguards. In such experiments as I have described, subjects are given a task to perform, and changes in their performance are regarded as favourable within the particular test situation. Whether the effects appear desirable or not depends largely on the situation in which a subject's activity is observed, and the subject who has taken amphetamine usually judges the effects more favourably than the experimenter. For instance, an increase in speed with only a small loss of accuracy may be regarded as a favourable effect in a test-situation in the laboratory, but would not be so regarded if the subject were driving a car in everyday circumstances. Similarly, the way in which a task holds the attention may be favourable in terms of test-scores, but may lead an individual to persist inappropriately in activities which are not rewarding. For instance, a research colleague, left to his own devices after a dose of amphetamine, spent a morning preparing with great thoroughness a grandiose research-plan, of which he would never find time to carry out even a quarter. Moreover, the tests in which favourable effects may be observed provide subjects with scope for their energies and allow a considerable degree of success. The effects are less favourable if this is not so, or if activity is more constrained by the test-situation. Then impulsive and inappropriate activity is often observed, and subjects tend to become irritable and restless. When one activity competes with another, and separate responses have to be made to more than one stimulus at much the same time, the effects of the drug tend to be unfavourable and behaviour disorganized.

PSYCHOLOGICAL PROBLEMS IN FLYING PERSONNEL

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The realization of the importance of personal predisposition to neurosis emphasized the potential value of psychiatric selection, and sufficient data are now available to show the actual value of such a procedure. In the urgent circumstances in which aircrew were recruited and trained in the earlier part of the war, it was impossible for the trained psychiatrists available to interview more than a minute fraction of the intake. An important lesson of the war has been that, if psychiatric selection of aircrew is to be successful, the selecting psychiatrists must themselves be selected for their aptitude for that particular task, for diplomas and success in other fields of psychiatry are not enough.

To restore balance to this sketchy survey of the psychiatric problems in aircrew in Bomber Command, it must be asserted that the important work in this field took place on the airfields themselves. And it was carried out by the commanders of flights, squadrons and stations, with the valuable help of squadron and station medical officers. These men, by constant contact with the dangers of operational flying and with the effects of these dangers upon aircrew, learnt much about the psychiatry of fear, and applied all they knew.

Furthermore, although, by administering 15 mg. doses, the effects which I have described may be obtained in about half of a group of healthy subjects, less-desirable consequences may follow in the other half. Individual differences are large and unpredictable, and the effects differ in the same individual from occasion to occasion. Sometimes individuals become excited, restless and garrulous. Some become irritable and quarrelsome, others emotionally labile. For instance, a normally well-balanced girl carried out a psychomotor test after a 15 mg. dose. She started brilliantly, and it seemed probable that she would beat the laboratory record. She made a few unlucky errors, however, burst into tears, and was quite unable to complete the test. Irresponsible behaviour, euphoria and airy, dreamy or drunk feelings may also result from a 15 mg. dose. Undesirable bodily effects, such as tachycardia, precordial discomfort, headache, giddiness and nausea, are also relatively common.

I have described the effects of a relatively large dose of amphetamine, because it is necessary to administer a dose of this size, if by present methods satisfactory observations of the effects on performance are to be made. The effects of 5 mg. and 10 mg. cannot be described so definitely. The desire for sleep, however, is appreciably reduced even by 5 mg. The same dose, or 10 mg., may produce definite changes in feeling-tone, but changes in test- and other behaviour, are not often observed. On the whole, the desirable effects are more prominent than the undesirable, but even with these doses the undesirable effects are not negligible.

The Germans explored the military use of analeptic drugs such as amphetamine and desoxyephedrine (" Pervitin ") before 1939, and at first their reports were favourable to its use. Desoxyephedrine was used fairly widely both by german soldiers and civilians at the beginning of the war. In Britain, systematic research into their military use was started in the summer of 1940, and was continued fairly intensively for about two years. Since then research in this field has been desultory. Even in 1940 there was an extensive published literature dealing with the effects on the behaviour of healthy individuals, but then, as now, it abounded with contradictory findings in respect of important details. Relatively large laboratory- and field-trials of amphetamine were staged in Britain, and, as a result of these trials and of the reports in the literature, it was concluded that the favourable effects of the drug did not generally outweigh the dangers, and widespread usage of the drug was strongly discouraged. A limited use in special circumstances in order to reduce the desire for sleep was reluctantly allowed. Thus, a small dose (e.g. 5 mg. amphetamine) may be administered on occasions, but not as a routine, to drivers who have to travel a long distance at night, but who are not adequately trained. In other circumstances, when it does not matter that judgment becomes impaired, larger doses may be administered for the sake of the mild elation produced by the drug.

I am sure that this policy was correct, and I think that those responsible for it would make little change in it now, although the perspective in which these matters are seen has changed considerably in the interval. Personally, I would place more emphasis now upon the fact that the benefits claimed for the drug are obtained by training and by other measures which lead to good morale. Also the dangers of creating a habit of dependance upon drugs were perhaps underestimated. Certainly the Germans are reported to have encountered a number of adverse effects from habit-formation. Their early reports were far less moderate than ours, but after 1941 the trend of their opinion changed, and the dangers of desoxyephedrine rather than the benefits were stressed. For instance, they reported cases of severe nervous illness, developing in individuals who attempted by the unwise use of desoxyephedrine to restore confidence when it was impaired as a result of stress. Some individuals come to rely upon these drugs whenever they have to face difficulties, although they may take only a small dose. Chronic over-workers may take them to revive flagging energies. There is also evidence of a persistent craving for stimulants of this kind, particularly in Germany amongst the apathetic and frustrated of the professional classes.

Experiments on the Causes of Errors attributed to " Fatigue "

Let us now consider the case for the administration of amphetamine to pilots and other aircrew, when they are engaged upon a lengthy flight. Actually, analeptic drugs were officially banned for aircrew, except in rescue-dinghies, because of the danger that doses sufficient to be beneficial would also impair judgment. The argument in their favour might be baldly paraphrased thus : " A long flight is fatiguing, and aircrew become more liable to make mistakes as they become fatigued. Amphetamine may sustain them and reduce the number of mistakes due to fatigue. Fatigue may be likened to a fire burning dim, because it is choked by ashes, the products of its metabolism. Amphetamine acts like a bellows."

This argument is a misguided one, becauses it assumes that an important cause of mistakes by aircrew is fatigue, whatever fatigue may mean. The indiscriminate use of this term is indeed a source of confusion which has retarded the solution of a number of practical problems of the kind which we are now considering. One may dispense with the term, however, and ask under what precise conditions errors occur. Two independent lines of investigation pursued during the war provided approximate answers to this question. These I shall now describe very briefly.

The Cockpit Experiments

At the beginning of the war, a new approach to the problem of so-called " pilot-fatigue " was made possible by the development by the late Dr. Craik of an apparatus which is now called the Cambridge Cockpit. This ingenious apparatus provided the means of analyzing in detail the performance of pilots engaged in an instrument flying-exercise. The Cambridge Cockpit was something like a Link trainer, but it was stationary and included devices by which detailed graphic records were obtained of the movement of instruments and controls.

Since the control of the machine was difficult and the exercises were prolonged, it was expected that the skill of the pilot-subjects would become gradually disorganized. This proved to be the case. It was no explanation of the disorganization to attribute it to fatigue, however, and further experiments had to be carried out to discover the

reasons for it. These facts were established (Davis, 1946, and in press):

i. If in an individual case disorganization of skill occurred, it occurred relatively quickly and was definite at the end of 20-30 minutes. If at the end of 45 minutes an individual was maintaining a high standard of performance, he would continue to do so for several hours, much longer than the time for which the test usually lasted.

ii. If skill became disorganized, the effects showed two phases. In the first phase, there was an increase in the force and extent of responses to deviations of instruments from prescribed readings and an increase in inappropriate, restless movements. In the second phase, activity was reduced and insufficient.

iii. Disorganization of skill was associated with emotional disturbance. In the first phase, subjects were irritable, excited and anxious, in the second phase apathetic and discouraged.

iv. The degree and type of disorganization was dependent upon the grade and type of predisposition to neurotic breakdown under stress, as assessed at an independent psychiatric interview.

v. A similar disorganization of skill may be produced in simple test-situations, when stimuli are of short duration and when fatigue could not be present.

From these facts it was concluded that in the experimental analogue of flying, disorganization of skill was not determined primarily by prolongation of the test, but was due mainly to the anxiety provoked by the test. Other experiments indicated that, in the case of the cockpit-test, anxiety was due to the difficulty experienced by predisposed subjects in attaining a satisfying standard of performance. The machine was very unstable, and excessive activity was penalized heavily. These characteristics made some subjects feel insecure, particularly if they aspired to a high standard of accuracy. It was concluded that the general conditions of disorganization of skill are factors in the environment which signify danger and evoke in the subject anticipatory tension, the subject not having the means of removing the danger and thereby relieving the tension.

Direct Observations

These results agreed with the results of investigations carried out by a branch of the Medical Directorate of the RAF. From conventional views on fatigue it would be expected that, as the length of flights increased, so accidents would become more common. Professor Bradford Hill and Wing-Commander G. O. Williams overcame the difficulties of comparing the incidence of landing-accidents with different lengths of operational flights, and showed that, contrary to these views, landing-accidents were not more frequent after long sorties than after short ones, with the possible exception of flights of more than 10 hours.

Similarly Squadron-Leader D. D. Reid showed that, in the air, errors by navigators, whose efficiency was more easily assessed than that of pilots, did not become more frequent with the length of time at the job. On the contrary, the peaks in the incidence of errors corresponded to the times at which emotional stress was likely to be at its highest, as, for example, when crossing the well-defended areas near the coast of enemy-occupied territory.

Reid also showed that the incidence in aircrew of acute neurosis, which is sometimes said to be due to fatigue, was correlated relatively highly with measures of the hazard under which sorties were flown. It was not correlated, however, with the number of sorties or the amount of flying within a given period, as would be expected if "fatigue" was an important factor in the causation of such neurosis.

Both series of investigations incriminated stress and the resultant anxiety, rather than prolongation of work and fatigue, as the conditions under which errors are made. Many of the arguments, by which the use of amphetamine by aircrew is justified, are therefore irrelevant. It is, then, not sufficient only to study the effects of amphetamine or other remedies. One must learn something of the reasons for the human failings, which such remedies are said to prevent. Studies of the disorders of skill are still being pursued in this laboratory.

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WARTIME INVESTIGATIONS INTO SEA- AND AIRSICKNESS

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In 1914, shortly after a raiding party—Commandos as such people were beginning to be called—had set out to raid the Lofoten Isles, the expedition ran into bad weather, and the ships had to delay to effect repairs. In the opinion of some on board, the necessity for repairs was providential for, had it not occurred, the seasickness of a large number of the Commandos would have seriously hampered the expedition. Fortunately for the success of the operation, the stormy weather had subsided by the time the repairs were completed, and the seasickness abated.

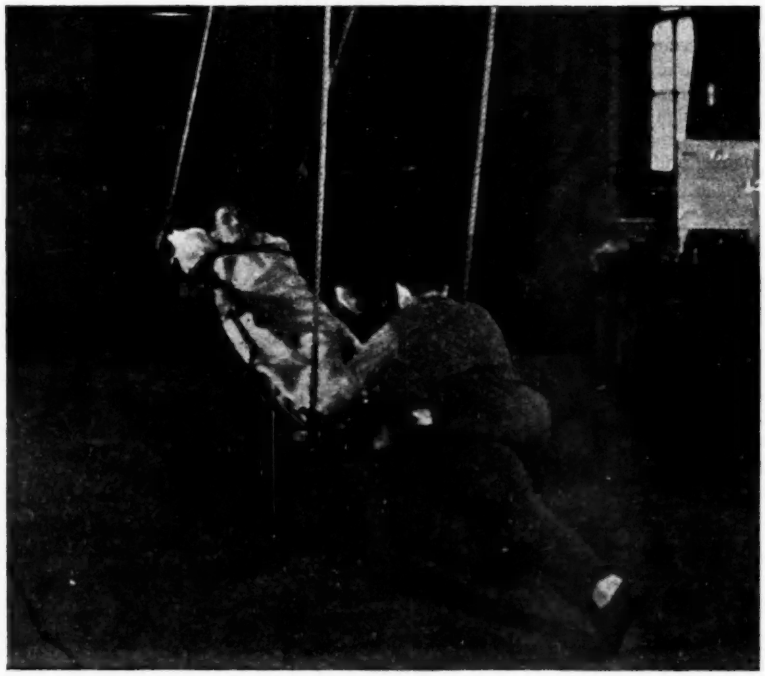
However, the warning that seasickness might prove a hazard in air-sea-land operations was heeded, and the search for an effective seasickness remedy began. Previously the Flying Personnel Research Committee had instituted a programme of research into the prevention of airsickness, and together with the Military Personnel Research Committee similar research into seasickness was undertaken. The problem was tackled by teamwork, and it is impossible to state where one person's work began or ended. Laboratory work was carried out in Dr. E. A. Carmichael's department at the National Hospital, Queen Square, London, and at the National Institute for Medical Research at Hampstead, and much work was done in the field with the co-operation of the three fighting services. Major J. A. Magladery, R.C.A.M.C., Dr. G. L. Brown, and Dr. B. McArdle originated work in the laboratory (using a large swing to produce motion-sickness). Dr. McArdle, joined by Surgeon Lieutenant-Commander Holling and Major Trotter, carried on the investigation at sea, Major Magladery and Squadron-Leaders Joekes and Parkes continued investigations pertaining to airsickness. Major Clifford Wilson carried out field-trials of the effects of certain drugs used on military efficiency. Dr. Harold King and Dr. H. Mackintosh advised on pharmacological questions, and Professor Bradford Hill gave invaluable co-operation throughout in the statistical evaluation of results.

Swing-Sickness

When time is not important, it would be possible to deal with those susceptible to motion-sickness either by habituating them to the actual motion or by gradually eliminating them from the combatant unit. This could not be done in 1941, because it was necessary to train large numbers of landsmen, and only few planes, gliders and landing-craft were available. At this time Major Magladery suggested that the use of a swing might provide a useful means of testing the susceptibility of the men to motion-sickness, of immunizing them to its effects, and of studying the problem of motion-sickness in man and in animals under laboratory conditions.

A swing was accordingly built (fig. 1) and was found to be successful in reproducing the symptoms of sea- and airsickness; so it seemed that the necessity of having to wait for suitable weather, available craft and co-operative men to be all together at the same time could be avoided. The swing was simple both to construct and to manipulate, and in practice proved to be as capable of producing motion-sickness as any of the more complicated means which have since been devised. The relationship between swing-sickness and air- and seasickness was examined by finding whether men susceptible to the motion of a swing are equally susceptible to the motion of an aeroplane or ship. Unfortunately it was found that swing-sickness could not be regarded as identical with either seasickness or airsickness, for the same man might be sick on the swing and not on the sea, or sick on the sea and not sick on the swing. It was found that a considerable proportion of men susceptible to swing-sickness was also susceptible to sea- and airsickness, but it was clear that to use a swing-test as a means of eliminating potential sea or air sufferers would be too wasteful of men. It was

FIG. 1. SWING FOR REPRODUCING SYMPTOMS OF SEA- AND AIRSICKNESS



also found that, to use the swing as a means of immunizing susceptible subjects to the effects of motion, though it could be done in some subjects, was too doubtful and time-consuming a method to be generally recommended. So it was that the swing offered no immediate practical application to the reduction of motion-sickness, but did, however, enable workers to advance our knowledge of the pathology and therapy of the condition.

It was found possible to record the contractions of a subject's stomach whilst he was actually being swung. This was done by letting him swallow a balloon attached to a recording device by a long length of rubber tubing. In this way it was possible to show that the stomach four hours after a meal shows slow rhythmical contractions with the effects of respiratory activity superimposed on them. When swinging starts in a susceptible subject, the rhythmical activity ceases, and the intragastric pressure falls as the subject becomes nauseated. These effects, together with the decreased amplitude of the respiratory excursions, continue for some time after swinging has ceased, while the subject lies on the swing feeling miserable. This atony of the stomach has also been seen radiographically in susceptible, but not in immune, subjects. Tight binding of the abdomen is not successful in counteracting it, and though intravenous injection of 0·5 mg. prostigmin and 0·4 mg. atropine causes powerful hunger-contractions and increased gastric tone in resting subjects, it fails to prevent the fall of gastric tone when a susceptible subject is swung, and moreover, it has no specific effect in preventing motion-sickness.

Manning & McIntyre (1943), as a result of experiments on the swing, have presented evidence to show that the position of the head relative to the resultant of the forces involved is an important factor in determining the development of swing-sickness. When the resultant of the forces involved acts perpendicularly to a line between the outer canthus of the eye and the auditory meatus, the incidence of swing-sickness is high, but when the resultant force acts parallel to this line the incidence is low. These findings may prove to be of value in the prevention and nursing of those suffering from motion-sickness.

Other experiments suggested that nausea caused by the swing had a slight effect in reducing performance on a " psycho-motor " testing machine designed by Dr. Schuster. This effect, however, was of short duration.

Transatlantic workers have furthered the study of swing-sickness, particularly in animals, by cortical-ablation experiments and the recording of action-potentials from various parts of the central nervous system as the animal is being swung. Others have used the method in the search for newer and better drugs in the treatment of motion-sickness.

Sea-Trials

As it became established that neither the swing nor any other available measure could serve as an effective means of eliminating susceptible personnel from sea- or airborne operations or of accustoming the participants to the incidental movements, it became obvious that drug therapy as a means of reducing motion-sickness would have to be considered. At that time, 1941, no one knew enough to say which of the many remedies recommended as certain cures of seasickness could be given to combatant troops with the possibility of doing any good and the certainty of doing no harm.

Hyoscine has always been used in the treatment of sea-sickness, but the state of knowledge in 1941 was that hyoscine was only one of many recommended remedies; for example, if one judged by the reports in the literature there was nothing to choose between hyoscine, chloral, chloretone, amytal, apomorphine, syntropan, amphetamine, ergotamine, ammonium chloride, glucose or numerous other remedies. Subsequent observations showed that these latter drugs had little or no beneficial action on motion-sickness. It was not, even in 1941, generally held that seasickness might be controlled by drugs, for some enthusiasts pinned their faith to a belladonna plaster applied to the abdomen; a constricting band to the neck, chest, or belly; a device to keep the head in one plane; or some, more understandably, to a régime of stout, neat brandy, iced ginger-ale or sips of iced champagne; it has always been regretted by the observers that the inapplicability of these last measures to combat troops prevented a trial of them being carried out !

To those who know the difficulties of getting trustworthy answers from trials requiring the administration of drugs to military personnel, it is very understandable that misleading reports of the efficacy of sea- and airsickness remedies should have appeared. The peacetime ship's surgeon is not in a position to treat his patients as experimental subjects and consequently cannot carry out trials under conditions which permit of scientific control. Nevertheless in the literature of seasickness there were occasional papers which seemed to give trustworthy information of which drugs might be worth trial. Such recommended drugs were either sedatives or drugs of the belladonna group. When the time came to select drugs for trial, it was deemed advisable to include proprietary drugs because there were claims that the synergistic action of the constituents of certain proprietary formulæ caused them to be more efficacious than the total separate actions of the constituents. No reliable evidence of this synergism has been obtained.

Though some indication of the efficacy of the remedies on trial might be derived from a study of their effect on swing-sickness, for a true assessment it was necessary to carry out trials at sea and in the air. For this purpose it was necessary to find vessels which would be permitted to go to sea in rough weather, and this appeared to preclude landing-craft. This was unfortunate, because it is always desirable for an investigator to have first-hand knowledge of all aspects of the problem he is investigating. As an example, one may cite the finding of Major Magladery of the adverse effect of having to crouch to look out of the porthole of a glider, and the subsequent finding by Jowett & Thomson (1943), and Tyler (1946), that the elimination of excessive crouching in landing-craft reduced the amount of sickness.

However, eventually mine-sweepers working from Falmouth were the craft used to study seasickness. When the weather was rough, the minesweepers could not carry out their normal duties, and were willing to make special trips to sea for the benefit of the investigation. The majority of men enjoyed the trips, even though they might be sick, for a sea trip was a pleasant change from the intensive training they were undertaking at the time. Moreover since the men embarked with an air of secrecy carrying martial weapons, they were sometimes mistaken by onlookers for a commando raiding party, a mistake which pleased the men.

During the period of sea trials a party of 70 men embarked in two minesweepers whenever there was a prospect of rough weather. One hour before embarkation, each man

received either one of the drugs being tested or a dummy tablet. Tyler has subsequently shown that the incidence of sickness in military subjects is not significantly different whether they are given a placebo or not—indicating that the psychological effect of a placebo is negligible in such instances. Every precaution possible was taken to ensure that the drugs were in every case swallowed by the men, and though on occasions a pill was spat back into the drinking-mug used, most of the tricks to avoid taking a pill had been foreseen and prevented. The distribution of the remedies was planned to ensure a random distribution amongst the soldiers of the dummy tablets and the drugs under test. The trips to sea lasted up to 6 hours and the men had free range of the ship, though they usually preferred to remain on deck.

At least one observer sailed with each ship. He kept a record of the trip, including a note of the type of motion encountered, but his main purpose was to talk to the men individually and to observe and record the onset of any sickness. In this way, occasional cases of nausea which had escaped observation were brought to light. In very rough sea, up to 40 % of the men on board were affected, and trips in which little or no sickness took place were not included in the series. In an attempt to grade the severity of conditions in the different trips, records were made with instruments designed to record the frequency and extent of the ship's movements. These were not satisfactory, and it was concluded that the most practical method of measuring the severity of a ship's motion was to use the incidence of sickness occurring in the group which had received only placebos.

Results

In estimating the effects of the remedies, both those who had vomited and those who had experienced nausea were included in the description "sick". The diagnosis thus rested mainly on a man's own statement, but was usually confirmed either by seeing him vomit or noting his haggard look and greenish pallor, for the observers quickly became skilled at recognizing the early signs of seasickness. Nauseated subjects were included as sick because, on short cross-channel trips, nausea alone might be just as incapacitating as vomiting. Moreover, the fact that the majority of those nauseated had vomited by the end of the trip suggests that vomiting may be regarded as an incidental symptom likely to occur sooner or later in a nauseated subject. It is of course true that, on long voyages, continued vomiting causing loss of food and fluid may exhaust the sufferers, but it was considered that for military purposes nausea was just as undesirable as vomiting.

The results of early trips in which proprietary remedies were used are shown in table I.

The final column of the table gives a figure which enables a rough comparison to be made between two drugs, even though one might have been used on a rough trip and one on a comparatively smooth trip. It estimates the number who were saved from being sick by the effect of the remedy, and is expressed as a percentage of the total number of those who would have been sick if no drug other than a placebo had been given. Thus when Remedy C_1 is under consideration, 34 % of the controls were sick, but only 16 % of the treated. It is assumed that 34 %−16 %, *i.e.*, 18 % of all men

TABLE I. RESULTS OF USE OF SEASICKNESS REMEDIES

Drugs	Trips	Number of controls	% Sick	Number of treated	% Sick	% Susceptibles protected
Remedy A	1–7	83	22	78	22	0
Remedy B	1–7	83	22	75	25	0
Remedy C_1	1–10	141	34	129	16	53
Remedy C_2	13–17	86	38	91	37	3
Methedrine (8 mg.)	1–7	83	22	77	22	0

$$\%\text{Susceptibles protected} = \frac{100(\%\text{ sick in control-group} - \%\text{ sick in treated group})}{(\%\text{ sick in control-group}).}$$

receiving C_1 were protected, so that 53 %, that is $\frac{18}{34} \times 100$ of those who would otherwise have been sick were afforded protection. This figure gives only an indication of the order of efficiency of a drug, and is not an exact statement. It would be invalidated in comparing remedies used on trips of different roughness, if it were subsequently found that the efficacy of a drug varied with the severity of conditions. It was used in order to be able quickly to reject remedies which did not appear promising.

From these results it appeared that remedies A (containing chloretone), B (containing syntropan) and methedrine (equivalent pharmacologically to amphetamine) showed no significant effect in preventing seasickness. C_1 (containing hyoscine) showed a significant effect in preventing seasickness, but a second sample of the same remedy C_2, which the makers said was identical with the first sample, was found to be without significant effect. Fortunately it was the first sample which had shown effects, so that the observers were encouraged to search for the active principle.

Table II shows all the remedies tested in this series arranged in the approximate order of their efficacy :

TABLE II. SEASICKNESS REMEDIES TESTED, ARRANGED IN ORDER OF EFFICACY

Drug	% Susceptibles protected
Hyoscine 1·2 mg.	73
Hyoscine 0·6 mg.	57
Remedy C_1 (hyoscine + hyoscyamine)	53
Atropine 1 mg.	40
l-Hyoscyamine 0·96 mg.	40
d-Hyoscyamine 2 mg.	25
Homatropine 2 mg.	25
Phenobarbitone 1 grain [66 mg.]	18
Sodium hydantoinate 0·2 g.	8
Remedy C_2 (? composition)	3
Remedy A	0
Remedy B	0
Hexobarbitone (evipan) 10 grains [660 mg.]	0
Methedrine 8 mg.	0

It is obvious from this table that drugs of the belladonna-scopolamine group have a significant effect in preventing seasickness. Statistical analysis of the material shows that the evidence is also very suggestive that hyoscine (especially in the dosage of 1·2 mg.) is more effective than hyoscyamine or any similar drug. Subsequent work, in particular by

Hill & Guest (1945) in India, and Tyler (1946) in California, who actually made use of assault-craft, has confirmed these findings. The effect of the remedies has also been observed on longer trips to sea, and it has been found that hyoscine given in an original dose of 0·6 mg. can be repeated in doses of 0·3 mg. at intervals of 6 hours without the appearance of obvious side-effects.

The observers on airsickness have found it very difficult to obtain comparable figures; this is largely because of the impossibility of accommodating sufficiently large groups of men in aeroplanes to subject them to the same conditions at the same time. Such figures as there are indicate that, although hyoscine is effective in preventing some airsickness, its value is not as great as in seasickness.

Other remedies have been developed by the RAF, the Royal Canadian Navy, and the American Army. All three of these remedies contain a number of drugs and include hyoscine. The general opinion at present is that there is nothing to choose between hyoscine itself and any of the more complex remedies containing it, but that no known remedy will protect every person in all weathers.

In general, careful observers of motion-sickness occurring in military personnel have not been impressed by the evidence that psychological factors play any significant part in the genesis of true motion-sickness: in military subjects air- and seasickness appear to be almost wholly a function of the physical conditions present at the time.

From table II it will be seen that phenobarbitone appeared to have some protective effect. The investigation of this and similar drugs was not pursued at the time because it seemed that the belladonna-scopolamine drugs were so much superior, but Tyler (1946) has subsequently confirmed this observation of the beneficial effect of some barbiturates and has shown that they are effective only when conditions are moderate. Independently, canadian workers have pursued this investigation of barbiturates, and the public announcement of their findings is awaited with interest. Whether a barbiturate more effective than hyoscine is discovered or not, the combination of barbiturate and hyoscine should be considered for civilian use, since a possible hypnotic effect of barbiturate, however undesirable in military use, might be welcomed in civilian practice.

The only unpleasant side-effect of the use of hyoscine in these doses was the occasional complaint that the dryness of the mouth made mastication difficult. This side-effect was still more marked with hyoscyamine; recent work having shown that, weight for weight, hyoscyamine depresses salivation five times as much as hyoscine. No drowsiness and no effect on visual accommodation was found, and no evidence was found that hyoscine in these doses had any effect on military efficiency; indeed there are reports that hyoscine may slightly improve shooting-performance.

The Use of Seasickness Remedies on Active Service

Though seasickness remedies were used on D-day in Italy and Normandy, it has proved extremely difficult to obtain authoritative reports of their effect when used in actual operations. This is because, in such circumstances, the observer is confined to a small group—one glider, landing-craft or aeroplane—and has more important matters to attend to. Good and bad reports have been received, but it is mostly the bad ones that have been published; the *Daily Express* quoted a War Office Brigadier as stating that D-day had resulted in the greatest mass vomiting ever known in the history of mankind. At the same time the late Ernie Pyle, the american war correspondent, reported that the result of taking the official seasickness remedy was almost to kill him.

> " The capsules," he reported, " have a strong sleeping powder in them, and by noon all the Army personnel aboard were in a drugged stupor. The capsules not only put us to sleep, but they constricted our throats, made our mouths bone dry, and dilated our pupils until we could hardly see. When we recovered from this insidious jag, along towards evening we threw all our seasickness remedy away, and after that we felt fine."

Then he adds, somewhat illogically for his castigation of the remedy, " Although the Channel crossing was rough, I didn't hear of a single man aboard who got sick." It appears that Ernie Pyle and his companions had taken at least twice the official dose. His story, nevertheless, brought criticism of the authorities who could allow the administration of such drugs.

This is one of many reasons why one should consider whether it is advisable to undertake routine administration of seasickness drugs to troops engaged on combined operations, since, whether it is effective or not, the drug is liable to be blamed for any subsequent mishaps. Again, the effect of seasickness of comparatively short duration may be considerably overrated, for healthy men virtually make a complete recovery from the effects of seasickness within a quarter of an hour of the cessation of the causative motion, and general experience of manoeuvres with landing-craft exercises is that the men have recovered by the time the actual landing takes place. The experience of the navy is that it would be preferable to reserve the drugs to be given under medical supervision on the few occasions when circumstances warrant it, otherwise relying on the habituation of trained men to counteract any susceptibility to motion-sickness. Should habituation not develop, it would be preferable to remove men who are permanently susceptible from such duties, rather than that they should have to rely on a drug.

Further Outlook

The above consideration of the military value of seasickness remedies does not imply that the search for a remedy has been of no avail. The doctor, whether civilian or military, who is called upon to treat motion-sickness, will welcome the knowledge that remedies containing hyoscine are most likely to be effective, and in the swing we have an easily assembled piece of apparatus for the production and investigation of one type of motion-sickness. Further study of its effects may be expected to increase our knowledge of the physiology of the labyrinth, of body-righting reflexes, of nausea and vomiting, and perhaps to indicate methods of controlling them more effectively.

The belladonna-scopolamine alkaloids offer a field for search for an alkaloid which will have the effect of preventing seasickness, but which will not cause mouth-dryness. So far, experiments in this direction have not been energetically pursued. The demonstration of the value of the belladonna and scopolamine alkaloids leads one to wonder why they should be effective. So far as our knowledge goes, they do not appear to be general cerebral depressants in the doses

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WARTIME PROBLEMS OF GLARE AND DAZZLE

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Problems of glare and dazzle during the war can be roughly classified into three groups concerned with (i) devices to protect the eyes from excessive natural light, (ii) dazzle from gunflash, searchlights, etc., (iii) dazzle as an offensive or defensive weapon.

1. Protection from Excessive Natural Light

In the protection of the eyes against excessive natural light, the problems are not essentially different from those encountered in peacetime, but there are some special military circumstances which call for particular attention. The worst case is that of the anti-aircraft gunner who has to scan the sky in the neighbourhood of the sun, on the lookout for enemy aircraft, which frequently attack down sun. It is impossible to look at the sun with the naked eye, but any filter dense enough to enable one to look at the sun interferes seriously with the efficiency of scanning in other parts of the field. The late Dr. Craik (1943) examined a whole group of different filters, neutral and coloured, of different optical densities, and tested the range at which aircraft, receding from the observer, just disappeared from sight under daylight conditions. His results indicated reductions of range by the use of the filter, varying from about 5% reduction for a filter of 30% transmission, to about 20% for a filter of 5% transmission. These values referred to neutral filters and to brightnesses of 500 to 1,500 equivalent foot-candles[1] corresponding to regions of the sky not particularly near the sun. Orange or red filters had less effect on range.

As regards comfort in use (assessed partly by blink-rate), all the filters were found to be an improvement on the naked eye, the denser filters being most favourable. Gilded filters were found to be particularly good, possibly on account of reflection of the infra-red radiation, but heat-absorbing glasses were not outstanding. Craik found that the reduction of field-size produced by goggles had an important effect in improving comfort.

Another factor to be considered was the possibility that a filter which reduced the visual rays entering the eye might, nevertheless, pass sufficient heat-radiation to cause damage to the retina. That such damage can occur we know from cases of damage by scanning near the sun, not under eclipse conditions.

For anti-aircraft gunners it was necessary (*a*) to sacrifice some sighting-range to help scanning near the sun, and (*b*) to avoid any danger of retinal damage. It was decided to use a rather deep green protex glass with a visual transmission of about 9% and a total heat transmission of 0.6%. For general ground-duties under sun-glare conditions, and for aircrews, tropex or Crookes B2 with visual transmission in the range 12 to 26% were specified. Latest air trials in India suggest that 15% transmission is the most satisfactory value for these duties. As the ratio of the light-transmission to the total heat-transmission is an indication of the margin of safety of a glass against retinal damage by heat, it may be of interest to give the ratio for the glasses mentioned:

$$\frac{\text{Light-transmission}}{\text{Heat-transmission}} = \begin{matrix} 15.0 \text{ (protex)}; & 1.6 \text{ (tropex)}; \\ & 0.6 \text{ (Crookes B2)}. \end{matrix}$$

The filters so far mentioned were uniform filters which could be fitted in any standard goggle or sun-spectacle,

[1] [1 foot-candle = 10.76 metre-candles; 1 equivalent foot-candle = 10.76 equivalent metre-candles.—ED.]

WARTIME INVESTIGATIONS INTO SEA- AND AIRSICKNESS

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given, for if this were the cause of their action one would expect barbiturates to be more effective. Their action on the stomach does not appear to be directly implicated, for atropine is more active than hyoscine in this respect and yet has a lesser effect in relieving seasickness, and whilst the atropine-prostigmine mixture mentioned above was more effective than atropine alone in increasing gastric tone, it has not proved any more successful as a motion-sickness remedy. Nor does hyoscine appear to act by depressing the vomiting-centre or its efferent paths, for it was found that hyoscine has no marked effect in preventing the vomiting caused in man by intravenous injection of the minimal emetic dose of apomorphine. It may be that hyoscine acts by suppressing discordant impulses arising in the labyrinths and muscles and joints, but this possibility requires investigation.

It has also been remarked that the belladonna drugs effective in seasickness are also effective in parkinsonism. This disease offers an opportunity to study the effect of different belladonna-scopolamine-like drugs in the hope that one may be found which will free the rigidity of the muscles and yet not cause mouth dryness or paresis of the accommodation. If such a drug were found it might well prove to be more effective than hyoscine in seasickness. This suggestion for improving our knowledge of seasickness remedies is put forward because under conditions of peacetime practice it will be difficult to continue adequate clinical investigations into the therapy of the condition of sea- and airsickness.

In conclusion it is necessary to apologise to certain canadian and american research workers whose valuable work on motion-sickness during the war years has not been given recognition here. Report on this work has been omitted because it has been available only in documents which come under the wartime category of "Restricted".

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but there were many attempts to provide protection against excessive natural light by special devices. The simplest of all perhaps was the snap-down visor, a filter of low transmission fixed to the goggles, which could be brought into action for short periods at will. Another scheme was the use of a pair of superimposed polarizing filters which could be rotated, one with respect to the other, so that the amount of transmitted light was variable from a very high to a very low value. Heat-absorbing filters with a small blacked-out or very dense dot on the line of sight of each lens, arranged so as to occlude the sun's image, were also tried. In another device of the same kind, the two blank dots were replaced by a vertical bar and a horizontal bar on the lenses of the two eyes. In the binocular field this produced a cross, at the central intersection of which the external field was completely occluded for both eyes.

While all these devices had their advocates and critics, none of them represented a complete solution to the military problem.

2. Protection against Dazzle from Gunflash and Searchlights

The crew of aircraft caught in searchlight beams may be subjected to considerable dazzle, not so intense as to be painful (at practical heights, illuminations at the eye are comparatively low) but sufficient to interfere seriously with fully dark-adapted vision. The chief sufferer is the air-gunner in a bomber who is on the lookout for enemy fighters. The dazzle results from three causes: (i) physiological dazzle produced in the eye; (ii) physical veiling-brightness by light scattered in the windows of the aircraft; (iii) physical veiling-brightness by atmospheric scatter in the searchlight beam.

Investigation showed that all three causes produced effects on vision of the same order of magnitude, and frequently corresponded to veiling-brightnesses which greatly exceeded the brightness of the night sky. While the dazzle from windows could be reduced by the use of glass in place of perspex, and could be eliminated by the use of clear vision-panels, i.e., open panels, little could be done to restrict physiological dazzle, and nothing at all to reduce the beam-scatter.

Gunflash dazzle was mainly a problem for the physical chemists and workers on armaments-research, whose aim was to produce flashless propellants, flash-eliminators, etc. But other investigations, both field and laboratory, were made to help in developing methods of assessing the amount of dazzle produced and to increase knowledge of the extent and manner in which flash-dazzle interferes with the vision at night. We now have a general picture of the dazzle effect. With a small source of dazzle, continuously exposed, the effect on the vision of a neighbouring object increases rapidly as the angular separation between object and glare-source is reduced, and it happens that a very simple quantitative law obtains: at $\theta°$ from the dazzle-source, vision is impaired just as if a veil of light were thrown over the object, the intensity of the veil being proportional to the illumination at the eye from the dazzle-source and inversely proportional to the square of the angle $\theta°$. Moreover, if the dazzle-source is exposed as a flash, the recovery of each part of the retina follows the same time-course as if this so-called " equivalent " veiling-brightness (as given by the formula just mentioned) had been flashed on for the same time. This was a great simplification, as it enabled the effects of point-sources of dazzle in any position to be reduced to the case of a uniform flash over the whole field.

Complete sets of results were obtained showing how the visual threshold in the dark recovered from field-flashes, for intensities covering the whole of the practical range. With these data, it was necessary only to determine the physical characteristics of a gunflash—its angular extent, brightness, and duration—to predict the effect on vision under a wide range of conditions. The relevant physical characteristics could be determined by a photographic method, admittedly rather laborious. Two special points may be mentioned. Although the gunflash has a very high brightness, in some cases equivalent to a hundred or more equivalent foot-candles acting for 1 second (an intensity which is well in the region of daylight or cone-vision), the effect on subsequent recovery in the dark depends on the scotopic value of the light. This means that the measuring instruments for assessing the brightness of flashes had to have a spectral response-curve appropriate to the scotopic or dark-adapted eye. Colours of gunflashes are just sufficiently various to make this point worth taking into account. While the dazzle-effect on each part of the retina could be calculated, the extent to which a dazzled observer could sight on an object by using indirect vision and " looking round " the worst affected area was still uncertain. By actual sighting-tests in a laboratory simulation, it appeared that under typical conditions an observer could sight round the dazzled patch covering the foveal retina provided this did not entail indirect vision to more than about 3° from the normal direction of fixation. Thus, for a given brightness of dazzle-flash, the flash covering the fovea would have its full dazzle-effect on sighting only if its angular radius exceeded about 3°. For smaller flashes the disabling effect was progressively reduced.

For some weapons, particularly quick-firing weapons in aircraft, a direct measurement of the effect of gunflash was desirable. A simple instrument based on the principle of the reflector-sight was designed for this purpose by Dr. Goldie of the RAF Physiological Laboratory. The " target " object was reflected into the field of view by an inclined glass-plate through which a practically unimpaired view of the dazzle-flash and background was obtained by transmission. The time to recover vision of the object after dazzle was measured. While the results obtained show considerable individual variation, and may be affected by the sky-brightness, the fact that the instrument can be installed in the gunner's position, and can be used under conditions closely approaching the practical case, made it a very useful practical tool.

3. Dazzle as a Possible Weapon

The idea that dazzle could be used as a weapon was constantly recurring during the war. On a very bright moonlit night a pilot well caught in the beam of a searchlight is prevented by dazzle from seeing objects on the ground within some 2 miles [3.2 km.] of the searchlight. By constantly holding an enemy aircraft in several beams spaced at the corners of a square pattern of 4 miles [6.4 km.] side, we might expect to obscure the ground completely. To deal with a number of aircraft without having to sight searchlights on each, it was proposed in several schemes to instal powerful non-directional lights spaced in a pattern

over the whole countryside. Schemes of this kind fail for two main reasons: (i) because of the enormous amount of electric power demanded, (ii) because in the presence of cloud the light reflected back on the ground is insufficiently intense to make objects more visible than if the lights were extinguished. More-modest schemes were a little more hopeful. Experiments were made to see if comparatively weak, steady but directional lights of the type of motor-car headlights could be used at spacings of the order of 100 feet [30.5 m.] to provide a kind of dazzle-screen against ground attackers. It was found that such a screen, while of some value in concealing ground objects such as men, vehicles, low buildings, etc., produced a useful effect in only a limited period of about ½ hour during nightfall.

In another group of schemes, the aim was to destroy the dark-adaptation of enemy pilots attacking ships or bombers under conditions of low illumination. The method was to fire a powerful light-flash at some critical moment during an attack. Without going into details of the several schemes of this kind which were tried out, it may be said that they suffered from the following handicaps. With the highest practicable flash-intensities—from the ship or bomber, or projected to the neighbourhood of the attacking aircraft—useful dazzle could be obtained, if at all, only at very low levels of natural light, moonlight or less. Under these conditions, it is difficult or impossible to sight on the attacker for the correct timing and, possibly, directioning of the dazzle-flash. The dazzle-flash can at best give a temporary respite of a few seconds and, on the whole, the tactical value was small.

A dazzle scheme or, more strictly, a confusion-light scheme of quite a different kind, led to an interesting laboratory experiment. The Germans used a radio-controlled bomb for daylight attacks on ships, which could be turned to left or right, forwards or to the rear, during its descent. In this way aiming errors could be corrected. After bomb-release, the bomb-aimer was able to see the bomb and so correct its trajectory by the aid of a powerful flare fixed to its tail. The possibility was considered that similar flares might be shot up from the target ship which would confuse the bomb-aimer and upset the visual judgements on which his control depended. An optical simulation of the field of view of the bomb-aimer's sight was set up showing the target ship, the moving bomb-flare following its correct undisturbed projectory, and, when desired, a cluster of flares moving as they would do if shot up from the target ship. By a system of motor-driven mirrors in the apparatus the motion of the bomb-flare could be modified by the observer just as in practice by left-right, forward-aft controls.

The experiments consisted in comparing the accuracy of controlled bombing in the model (*a*) with no flares, (*b*) with confusion-flares in operation. Observers had to be trained in the control before a fair comparison could be made. Determinations were made of the distribution of bombing errors, (*a*) without control, (*b*) with control, (*c*) with control and confusion-flares. The results were fairly conclusive that the confusion-flares produced only a slight disturbance. This laboratory study enabled difficult and elaborate full-scale trials to be dispensed with, and at the same time indicated certain possibilities in the ground-training of personnel operating radio-controlled bombs.

On the whole, it may be said that dazzle as an actual weapon of war has proved disappointing, while in those cases where it interferes in some measure with efficiency it is not particularly easy to eliminate.

ACKNOWLEDGEMENT

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REFERENCE

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HEARING-PROBLEMS INVOLVED IN SYSTEMS OF INTERCOMMUNICATION

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The space at my disposal does not permit me to touch on all aspects of research work undertaken by the department of otorhinolaryngology of the RAF. I shall confine my remarks to some problems of noise which we had to study, the effect it has on personnel, equipment used, and the means we adopted to overcome these problems. It may perhaps be wondered how a department of otorhinolaryngology has become involved in the subject of intercommunication, so perhaps a few words on this subject may be helpful. The department is concerned not only with the clinical aspects of the speciality, but with all aviation problems involving hearing. An acoustics laboratory, staffed by technical experts, is an integral part of the department, and studies applied acoustics in the field of aviation-otology.

In modern combat-aircraft it is absolutely essential to have good speech-communication between the aircraft and the ground controlling-stations, between the crews of different aircraft, and between the individual members of the crews. This communication must take place over electrical channels involving microphones, telephones and amplifiers, and the success of an operation frequently depends on the accuracy with which information is passed through these channels.

There is present at all times in an aircraft the very loud noise from the engines and propellers of the machine. The intensity of this noise depends upon the aircraft, and usually lies somewhere between 105 and 120 decibels above threshold. It is therefore capable of causing permanent damage to hearing if adequate protection is not provided. Obviously, precautions must be taken to shield both the speakers and listeners from this noise as much as possible, and care must also be taken to ensure that the personnel selected for aircrew-duties should be capable of understanding speech transmitted through telephones in the presence of a background-noise of this type. It has been known for some time that individuals differ in their ability to understand speech in noisy surroundings, and that this ability is not related directly to acuity of hearing as measured by the ordinary threshold tests.

There are two lines of attack on the problem of improving the standards of speech-communication in the air. (i) The devising of selection-tests, to be administered at the selection-boards for aviation candidates, which would weed out those candidates who cannot understand speech in noisy surroundings. (ii) The provision of protecting devices, such as helmets fitted with sound-excluding telephone-holders, which are to be worn by all members of an aircrew in order to reduce the intensity of the noise actually reaching the ear and hence to reduce its masking effect upon speech. In this way it is possible to protect the hearing from damage caused by exposure to the loud engine-noise. It is necessary, in most aircraft, for the crew at some time to be supplied with oxygen. The mask which is used in conjunction with the oxygen-equipment, and which covers the nose and mouth, serves also to hold the microphone and to reduce the intensity of the noise entering the communication-channel via the microphone.

I will now describe in some detail advances made along these two lines during the war.

Hearing-Tests

Until very recently, the only test of hearing which every candidate for flying duties with the RAF had to pass was the 20 feet [6 m.] forced-whisper test. In this test the candidate had to be able to repeat, using each ear separately, a list of words whispered to him at a distance of 20 feet. An orderly stopped with his finger the ear which was not being tested. When carried out under the best conditions, this test gave an indication of the candidate's ability to understand very faint speech in quiet surroundings. In normal use, however, the results were apt to reflect differences in the background-noise present in the testing-rooms, in the accents of the testers, and in the lists of words which they are accustomed to use. At the best it did not measure the particular ability required of members of an aircrew, namely, the ability to understand loud speech in a background of loud noise. In other words it was not a standard test and it did not measure what was required.

In 1941 it was decided to set up an acoustics laboratory in the department of otorhinolaryngology at the RAF Central Medical Establishment with the task of devising a new hearing-test which would not have these disadvantages and which could be applied to the extremely large numbers of aviation-candidates who were passing through the medical boards at that time. The technical staff to work in this laboratory was transferred from the Radiotelephony Speech Unit of the RAF Fighter Command and consisted of a phonetician, a physicist, and an electrical engineer. The laboratory is fully equipped to reproduce under controlled conditions the noisy surroundings encountered in military aircraft and to perform noise-intensity measurements and analyses, speech-articulation tests, and a wide range of audio-frequency electrical measurements.

As a result of experimental investigation, in the course of which several thousands of RAF personnel were given speech-articulation tests in a background of engine-noise, a test was devised which, it is believed, weeds out those candidates who are likely to prove unsatisfactory as members of an aircrew. The development of this test was completed in the early months of 1943, and is now the official hearing-test for the flying branch of the RAF. The hearing-test is in two parts, which are known as the Hearing Efficiency Test and the Pure Tone Test. Both these tests are recorded on gramophone-discs, and can be given to a number of men, up to a maximum of 10, at the same time. A compact

form of testing equipment known as the RAF Gramophone Audiometer has been constructed for applying these tests. It is essentially a high-quality electric gramophone, which is calibrated every day in order to ensure that the intensity of the output-signals does not vary.

The Hearing Efficiency Test is a speech-sound articulation test carried out in the presence of engine-noise comparable in intensity and spectrum with that reaching the ears of the crew under normal flying conditions. The speech and the engine-noise are recorded on a gramophone-disc and are led together to both ears of the candidates under test.

The Pure Tone Test is a rough form of pure-tone audiometry and indicates whether a candidate's hearing is effectively normal in each ear at octave-intervals throughout the frequency-range 250-4,000 cycles per second. It consists of groups of pure tone " pips " at an intensity level of 20 decibels above normal threshold, for each of the frequencies 4,000, 2,000, 1,000, 500 and 250 cycles per second. The candidate is tested in each ear separately, and he has to count the number of pips in each group and write down his answers on the form provided. In order to pass the test the candidate must respond satisfactorily at all 5 frequencies in each ear. Women's Auxiliary Air Force (WAAF) personnel-selection clerks have been trained in the acoustics laboratory to apply these tests and to record the results on the candidates' medical documents. The servicing of the equipment is undertaken by the acoustics laboratory.

These tests have now been in use at the only Aviation Candidates Medical Board still functioning in the RAF for six months and have given satisfaction with the limited number of aviation-candidates being accepted into the Service.

Aids to the Protection of Hearing

The other function of the laboratory has been to assess the efficiency of various devices such as flying-helmets, headbands, etc., in protecting the hearing of flying personnel from damage caused by the intense noise. The standard method of measuring the protection afforded by such a device, say a helmet, has been to expose a person to a loudspeaker source of pure tones and to determine his threshold when exposed directly to the sound and also when protected from the sound by the wearing of the helmet. The difference in decibels between these two thresholds at each frequency gives a measure of the amount by which the helmet attenuates sound of that particular frequency. This method is rather tedious, in that the measurements, even with a single person, have to be repeated a number of times in order to get a stable mean-value of attenuation.

Because of differences in the way in which the helmet fits different persons the mean value thus obtained varies from person to person and it is necessary to test a fairly large number of persons and to express the results as a mean of the individual findings. This makes the comparison of different types of protective devices a very laborious and time-consuming business. In order to overcome this difficulty, a method of testing has been developed in the acoustics laboratory which enables a quick comparison to be made between different helmets. In this method, a microphone is mounted in a wooden head to serve as a dummy ear, and the voltages which develop across the microphone when the head is exposed to a source of sound are measured, first, when the head is uncovered and, secondly, when it is covered with the helmet. The difference once again gives the attenuation of the helmet at any particular frequency. These measurements can be made very quickly, and if care is taken to ensure that the pressure of the helmet on the head is constant, they are quite repeatable. It is true, of course, that the seal between the telephone-holder and the side of the wooden head differs from the seal achieved with the human head, with all its unevenness, and for this reason the subjective type of measurement may give a better representation of the average amount of protection which the helmet will give to the wearer. However, the objective method is an invaluable aid in the development of helmet-design.

At the beginning of the war the type B leather helmet was the only one available for flying personnel, but this has now been replaced by the type C helmet which is much more comfortable to wear and is available in leather for home use, or in cotton-drill for use in the tropics, or in aertex for use on long patrols, e.g., in Coastal Command, where comfort and lightness are of great importance. It was developed in the department of otorhinolaryngology, based on such data as head-measurements, noise-exclusion properties, comfort, etc. Experience over several years has shown that this type C helmet gives adequate protection to the hearing, and that, if the helmet is properly worn, exposure to aircraft-engine noise for the longest periods will not cause deafness.

Special classes of non-flying personnel, such as engine-test-bed operators, may be exposed to noise which is much more intense than that encountered in normal flight, and additional protection has to be provided to safeguard their hearing. This can take the form of earplugs or specially-designed headbands giving a high value of sound-exclusion. The laboratory has been able to give a considerable amount of help in assessing the performance of these earplugs and headbands.

It would seem that in the future the gas-turbine will have an increasingly important part to play in the development of combat-aircraft. The noise produced by this type of engine differs both in intensity and frequency-content from that produced by the ordinary reciprocating engine, and it is known that when the engines are accelerated with the aircraft on the ground the intensity of the noise in certain spots outside the aircraft may rise well above 130 decibels. It appears, however, that in the air the noise is much less intense and is unlikely to call for any change in the flying-helmet. An investigation into the character of the noise under different conditions is being carried out at present in conjunction with the Central Fighter Establishment.

The most direct approach to the problem of reducing the effects of noise on communication lies in the soundproofing of the aircraft, but unfortunately it is very difficult either to silence the engine without reducing its performance—or to soundproof the body of the aircraft—without adding considerably to its weight—and so this method has not had much application to military aircraft. It will, of course, be of great importance in the development of civil aviation, where the comfort of the passengers is of paramount importance.

NOISE AND HEARING IN RELATION TO THE PROBLEMS OF THE ROYAL NAVY

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In the Royal Navy, blast and gunfire are the chief causes of loss of hearing. While the gradual progressive deafness of cochlear type, commonly known as gunner's mate's deafness, and the injuries to the tympanic membrane with transient middle-ear deafness, are well known, the severe hearing-loss of cochlear type following a single instance of blast due to gunfire or other agent is not so well recognized.

FIG. 1. POSITION OF GUN-CREWS

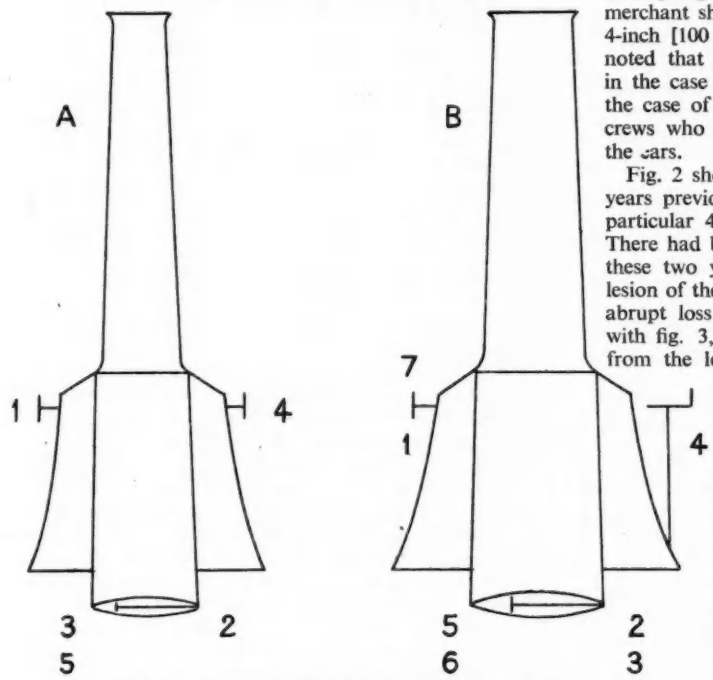
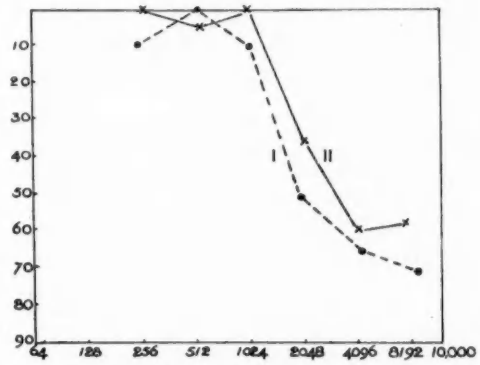


Diagram of (A) 12-pounder [5·4 kg.] and of (B) 4-inch [100 mm.] guns, the numbers showing position of the gun-crews (1-7)

In a series of 69 traumatized ears investigated by audiometry at a naval hospital (Suggit, 1943), 26 showed this type of loss. In another series of 139 audiograms of naval ratings rejected for submarine-detector duties by Surgeon Lieutenant-Commander Ransome-Wallis at H.M.S. *Osprey*, 62 showed this type of severe cochlear damage.

FIG. 2. BLAST-LESION OF THE COCHLEA IN A NAVAL-RATING



Ordinates : hearing-loss in decibels
Abscissae : frequency in double vibrations per second
I = right air-conduction'
II = left air-conduction

The majority of cases in the first series were naval-ratings undergoing training at a range for service as gunners in merchant ships. The guns used were a 12-pounder[1] and a 4-inch [100 mm.]. These are shown in fig 1. It is to be noted that no gunshields were fitted. Numbers 1 and 4 in the case of the 12-pounder and numbers 7, 4 and 1 in the case of the 4-inch gun were the members of the gun-crews who most frequently suffered from blast-injuries to the ears.

Fig. 2 shows the hearing-loss in a naval-rating who two years previously had been deafened by a round from this particular 4-inch gun while acting as No. 7 of the crew. There had been no subjective change in the hearing during these two years. It shows the characteristics of a blast-lesion of the cochlea with normal low and middle tones and abrupt loss of hearing in the high tones. This contrasts with fig. 3, which shows a gradual decline in hearing from the low tones where it is least, to the high tones where it is greatest. This is the progressive form of cochlear lesion or occupational deafness, and is due to repeated traumata of high-intensity sound or blast-waves, and not to a single blast-concussion. In this case (a naval-rating aged 36, who had been a gunner for two years only) a marked progressive deafness had supervened in a relatively short space of time. The period of development is usually much longer, and it has been said that we saw in senior officers and men in this war the effects of high-explosives in the first world war.

[1] [A gun firing a projectile weighing 12 pounds or 5.4 kg.—L.D.]

The protection used by the naval-ratings under training on this range was cottonwool wads. Eventually gunshields were fitted to these guns. From this date, the incidence of blast-deafness on this range fell rapidly. Instead of seeing some six cases of blast-deafness every week-end following the previous week's exercises, I saw hardly a case.

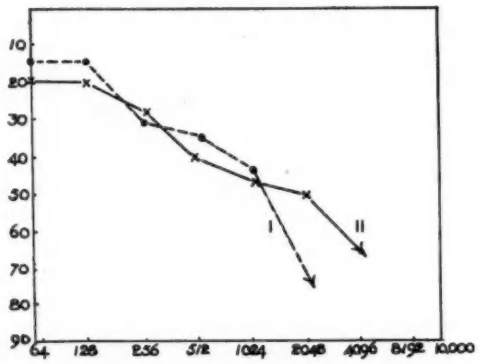
Fig. 4 shows a much more uncommon type of blast-deafness. It is essentially of middle-ear type, with the addition of a cochlear lesion in the middle tones as shown by the severe dip in the audiogram of bone-conduction in this zone. This lesion occurred 4½ years previously in an officer aged 31, who was near a motor-torpedo-boat when it exploded. Some improvement in hearing occurred in the first 2 months after injury, but since then the hearing had remained stationary.

An interesting experiment was carried out at H.M.S. *Excellent*, in which comparative tests with a dummy head incorporating a piezo-electric blast-pressure-gauge were made of the blast-protection afforded to the ear by a standard naval blast-helmet, an earplug, and service headphones. When the ear-passage faced towards the charge, the earplug reduced the pressure experienced at the position of the tympanic membrane from 4·5 pounds/inch² [0·3 kg./cm.²] to less than 0·1 pound/inch² [0·007 kg./cm.²], the headphones reduced it to about 0·7 pound/inch² [0·05 kg./cm.²] and the naval blast-helmet to about 3·3 pound/inch² [0·2 kg./cm.²]. Similar reductions in blast-pressure were obtained from the earplug and the headphones when the ear-passage was perpendicular to the direction of travel of the blast, but no appreciable reduction in the peak-pressure was obtained with the blast-helmet. An observation was also made with a wad of cottonwool in the ear-passage, the reduction in blast-pressure in this case being about 79 %.

These results are the reverse to those obtained in attenuation of the sound-waves produced by aircraft, as it has been found that the RAF flying-helmet attenuates sound to a greater extent than any earplug (Dickson & Ewing, 1941).

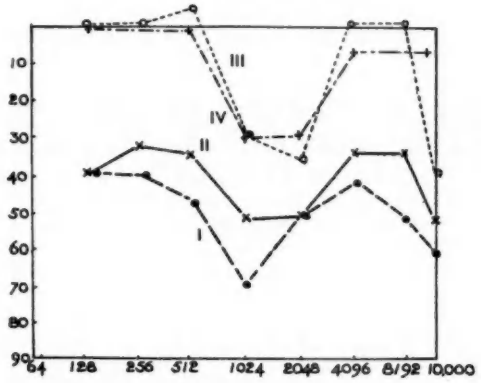
Loss of efficiency due to blast-deafness is always a serious matter, but is particularly so when naval-ratings trained in

FIG. 3. PROGRESSIVE FORM OF COCHLEAR LESION



Ordinates : hearing-loss in decibels
Abscissae : frequency in double vibrations per second
I = right air-conduction
II = left air-conduction

FIG. 4. BLAST-DEAFNESS OF MIDDLE-EAR TYPE



Ordinates : hearing-loss in decibels
Abscissae : frequency in double vibrations per second
I = right air-conduction
II = left air-conduction
III = right bone-conduction
IV = left bone-conduction

the operation of submarine-detector gear are concerned. These ratings are selected for their normal hearing and trained in the perception of sound of varying pitch and intensity. Ratings accepted as submarine-detector operators must have less than 20 decibels of hearing-loss for the frequencies 512 to 2896, and 30 decibels at 4096 cycles. They must also be able to distinguish a difference of + or − 30 cycles' change against a fundamental of 1,000 cycles.

Surgeon Lieutenant-Commander Ransome-Wallis carried out an interesting series of investigations on fatigue among submarine-detector ratings. The auditory threshold to sound-intensity was found to reach its peak in 15 to 30 minutes after listening commenced, and to show fatigue after 45 to 60 minutes. Recovery occurred after a further 15 minutes, but at the end of 2 hours a decrease in aural threshold was evident. Subjects with no previous experience were shown to reach peak-efficiency and to become fatigued at much the same rate as those with long operating-experience. A marked fatigue-factor in pitch-discrimination was also found. This was particularly evident in the second hour of the listening period. Fatigue in pitch-discrimination varied considerably among different individuals. As a result of these investigations the submarine-detector personnel were limited to watches of one hour.

One interesting point made by Surgeon Lieutenant-Commander Ransome-Wallis is that pitch-discrimination is normally better for notes of a lower frequency than for notes of a higher frequency than the reference note.

Gun-crews working in turrets are reasonably protected from blast-concussion, and for that reason the present-day policy of mounting the secondary armament, and also the guns of small ships, in turrets, has done much to reduce blast-trauma to the ears. Blast-deafness often occurred in men caught unawares on deck and other exposed positions. Submarine-detector personnel are therefore kept away from parts of the ship in which they are liable to receive blast-effects. Rubber earplugs, improved MSA (Mines Safety

Continued at foot of page 57

Notes on Contributors

DR. J. C. WATERLOW was employed during the war by the Medical Research Council in investigations on methods of increasing the efficiency of military personnel in hot climates. In 1943, with Dr. W. S. S. Ladell, he was sent to Iraq to study the problem of heat-stroke and heat-exhaustion. He is at present an assistant in the Medical Research Council's Human Nutrition Research Unit, and has been working on malnutrition of infants in the West Indies. His interest is in the common ground between physiology and clinical medicine.

DR. W. S. S. LADELL is attached to the Yaba Medical School at Lagos, where he is carrying on research into tropical physiological problems. He has previously contributed to the Bulletin a paper on "Thermal sweating" (*BMB* 735), and a note on his work has already been published.

SURGEON-LIEUTENANT COMMANDER F. P. ELLIS is the Secretary of a Sub-Committee of the Royal Naval Personnel Research Committee of the Medical Research Council which has been carrying out investigations since 1944 to determine the upper limiting levels of thermal conditions under which men can carry out the varying degrees of physical and mental activity normally necessary in warships without loss of efficiency or impairment of health. His past publications include papers on blood-transfusion, methods of oxygen-administration, and nitrous-fume poisoning, as problems of naval medicine.

DR. J. S. WEINER was a member of the Wartime Medical Research Council Team on Climatic Physiology at the National Hospital, Queen Square. He was previously engaged on the physiological study of high temperatures in South Africa and later at the London School of Hygiene and Tropical Medicine. He is at present Reader in physical anthropology in the University of Oxford, where he is continuing the study of adaptation of man to climatic extremes. His published work on high-temperature physiology includes investigation of the blood-circulation, sweating, kidney-function and efficiency.

DR. G. M. MORANT was formerly on the staff of University College, London, where he carried out researches in anthropology and statistics. He is now engaged at the RAF Institute of Aviation Medicine in applying the methods of those subjects to flying-problems.

DR. H. D. DARCUS is a graduate of the University of Oxford. He is at present a working member of the Operational Efficiency Sub-Committee of the Royal Naval Personnel Research Committee of the Medical Research Council. He is responsible for the investigation of the anatomical and physiological problems which arise in connexion with naval war-weapons. He is a member of the Anatomical Society of Great Britain and Ireland and is the author of "Some anatomical problems in naval warfare" (in press) as well as numerous confidential reports to the Medical Research Council.

DR. A. G. M. WEDDELL has previously contributed to the Bulletin a paper on "The anatomy of cutaneous sensibility" (*BMB* 733), and a note on his work has already been published.

MR. ALEC RODGER has been senior psychologist to the Admiralty since 1941. He is on loan from the National Institute of Industrial Psychology, to whose vocational-guidance staff he has belonged since 1929. He is a member of the Occupational Psychology Committee of the Medical Research Council, editor of *Occupational Psychology*, and honorary treasurer of the British Psychological Society.

WING-COMMANDER DENIS WILLIAMS has previously contributed to the Bulletin a paper on "The clinical application of electroencephalography" (*BMB* 613), and a note on his work has already been published.

DR. D. RUSSELL DAVIS is one of a group of workers in the Psychological Laboratory of the University of Cambridge who, with the support of the Medical Research Council, are extending the methods of experimental psychology to a variety of occupational problems. He qualified in medicine in 1938 and, after a short period in practice, returned to Cambridge University, of which he is a graduate, as a research student in experimental psychology. During the war he studied the causes of the errors made by pilots, and his most important researches have been made into the disorders of skill. Not only are these disorders pertinent to the causation of accidents, but by their study light may be thrown on the broader forms of failure of adaptation, which constitute neurosis. Several papers on these topics are now in course of publication.

DR. H. E. HOLLING is a member of the scientific staff of the Medical Research Council, and works at the Council's unit at Guy's Hospital. He trained at Sheffield University and is primarily interested in the vascular system. Holding a commission in the RNVR, he took a practical interest in naval problems during the 1939–1945 war. He was concerned in the prevention of immersion-foot, sea-sickness, body-wounds, toxic-gas poisoning, and heat-exhaustion. He collaborated in the writing of an Admiralty publication on the heating and ventilation of naval vessels. His published work includes papers on foetal plasma-proteins, the oxygen-usage of human muscle, vasodilator nerves in the human subject, urinary infections, cervical rib, varicose veins, shock, and methyl-bromide poisoning.

DR. W. S. STILES is a member of the scientific staff of the National Physical Laboratory. He has been concerned for some years with problems of physiological optics and with the performance of the eye under various lighting-conditions. His published work includes papers on the nature and effects of glare on the directional sensitivity of the retina, and the spectral sensitivities of the rod- and cone-mechanisms of vision. During the war he worked on methods of visual scanning, and other problems involving vision.

AIR COMMODORE E. D. DALZIEL DICKSON has been consultant in otorhinolaryngology to the RAF since 1938. He is in charge of an acoustics laboratory dealing with hearing-tests, effects of noise on auditory acuity and means of protection, etc., and is engaged in research problems in the field of aviation otology. He served with the RAMC from 1918–22 as ear, nose and throat specialist, joined the RAF in 1923, and has been engaged in surgical and ear, nose and throat duties at home and abroad. He served in the Balkans, Palestine, Middle East and Iraq. He is a Fellow of the Royal Society of Medicine, a member of its sections of laryngology and otology, and joint author of numerous papers in the *Journal of Laryngology & Otology* on various problems of aviation otology. A monograph incorporating most of these papers is in preparation and is to be published shortly.

MR. STEPHEN SUGGIT is surgeon in the ear, nose and throat department of University College Hospital, civil consultant to the Admiralty, larnygologist to London Chest Hospital and to Harefield & Clare Hall Sanatoria, and Surgeon Lieutenant-Commander, RNVR. He is a Fellow of the Royal Society of Medicine, being a member of its sections of laryngology and otology ; and is a member of the Association for Study of Diseases of the Chest and of the British Association of Otolaryngologists. His publications include papers on the variation in hearing in otosclerosis, and on deafness resulting from gunfire and explosions.

NOISE AND HEARING IN RELATION TO THE PROBLEMS OF THE ROYAL NAVY

Continued from page 56

Appliance) pattern, are now a general issue to all upper-deck personnel, and are a great advance on the wads of cotton-wool previously used.

Occupational deafness of cochlear type is also seen as a result of exposure to the noise of internal-combustion engines, that is, aircraft and motor-torpedo-boats and motor-gun-boats. In the case of air-crews, protection as in the RAF is afforded by headphones and flying-helmet. Engine-room ratings of small ships are issued with rubber earplugs.

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VOLUME 5 · NUMBER 1 · 1947
PART TWO · COMMENTARY
HISTORY · DOCUMENTATION

HITHERTO the Bulletin has contained, in addition to the scientific symposium which occupied the greater part of each number, subsidiary sections of bibliographical and historical interest. Starting with the present number, the Bulletin will be clearly divided into two parts. The collective monograph on a special subject which has become the characteristic feature of the Bulletin will constitute Part I. Part II contains miscellaneous articles on medical subjects of scientific, bibliographical, and historical interest. The book-review section will be extended and there will, as before, be sections devoted to historical notes, film-reviews, and lists of contents of current british medical and cognate periodicals. It is our intention that Part II should be a medium for extending the range of interest of each number of the Bulletin and for enhancing its continuity as a periodical.

CHARLES-VICTOR DAREMBERG 1817–1872
A great medical historian ... ... *A. Hahn*

MEDICINE IN CZECHOSLOVAKIA
Impressions of an english observer ... ... *A. Rides*

CARE OF CHILDREN
A critical review of the " Curtis Report " ... ... *C. McNeil*

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Historical Notes

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JOHN ATKINS: an eighteenth century naval surgeon ... ... *F. A. Tubbs*

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Physics for the anaesthetist—Short handbook of practical anaesthetics—Spuren von Stoffen entscheiden über unser Schicksal—Biology of cell tissues—Genetics for medical students—Problems of family life—The nervous child—Some minor ailments of childhood—Care of young babies—Preservation of proteins by freeze-drying—Medical aspects of growing old—Middle East science—Cultivation of viruses and rickettsiae in the chick embryo—Virus as organism—Textbook of bacteriology—Now for health—Men under stress—Introduction to clinical neurology—Lehrbuch der Augenheilkunde—Pathology of traumatic injury—Penicillin: its properties, uses and preparations—La pénicilline à la portée du praticien—Estado actual de la farmacologia arsenical—Histamina e anafilaxia—Descriptive atlas of radiographs—Handbook of radiography—Field service handbook of practical radiography—Manual of tomography—Neurosis and the mental health service—Tuberculosis in the West Indies—Re-adjustment in civil life of soldiers discharged from the army on account of neurosis—National health insurance in Great Britain 1911–1946—Health and social welfare 1947—Handbook for assistant medical officers of health on child welfare and school health work—La apendicitis en la primera infancia—Minor surgery—Surgery of the hand—Injuries and diseases of the oesophagus—Textbook of medicine.

Shorter Notices

Principles of anatomy and physiology for physical training instructors in the Royal Air Force—Demonstrations of physical signs in clinical surgery—Pye's surgical handicraft—El colapso circulatorio—Psychological medicine—Textbook of medical treatment—Edinburgh post-graduate lectures in medicine—Vers l'infiniment petit—Clinical practice in infectious diseases—Pulmonary tuberculosis—Aids to dermatology—Practical anaesthetics—You and your children—The M.B., B.S. finals—Pasteur—Aids to the diagnosis and treatment of venereal diseases—Ocular prosthesis—Aids to public health—Esquisse d'une histoire de la biologie—Histoire de la science—Aids to bacteriology—Diseases of infancy and childhood—Penicilina—El enclavamiento intramedular de Küntscher.

Books Received

Films

It's up to you
Your children and you
Scabies—1946
Penicillin in medical practice
Medical films from Australia

Guide to the Journals

There is a growing interest in the history of medical science, as of other sciences. Although Daremberg was one of the greatest of medical historians, his work has received relatively little attention in the english-speaking world, and it was for this reason that Dr. A. HAHN, Chief Librarian of the Faculty of Medicine, Paris, was invited to contribute the article below. Dr. HAHN refers to Daremberg's study of Galen by comparison of greek text and personal dissection. This indicates what the history of science might be—but seldom is!

CHARLES-VICTOR DAREMBERG 1817-1872

A Great Medical Historian

Dr. ANDRÉ HAHN

Wellcome Historical Medical Museum

" La chaire d'Histoire de la Médecine," wrote Jules Guérin in 1830 in his report on questions relating to the organization of the Faculty of Medicine of Paris, " doit, éclairée par l'esprit philosophique de notre époque, jeter le plus grand éclat sur la science et raviver des germes ensevelis sous des débris ignorés. C'est moins l'histoire des livres que des choses qu'elle aura pour objet; et, s'il est vrai que le cercle des erreurs soit aussi borné que le cercle des vérités, ce sera déjà rendre un grand service à la médecine que de l'avertir et de la garantir par les révélations de l'histoire, du retour des erreurs passées."

These lines, written 8 years after the suspension in 1822 of the course in medical history and the consequent retirement of its head, Jacques-Louis Moreau (de la Sarthe), the librarian-professor, showed how essential the study of the history of the medical sciences, which was later to be so neglected, was considered at that time. It was, however, not until 40 years later, on 9 March 1870, that the Faculty finally achieved the inauguration of the new school ; this was after a legacy of 150,000 francs had been left to the Faculty in 1869 by a former Master of the Requests to the Council of State, M. Salmon de Champotran, who was struck by the inadequacy of the historical side of medical education, and had in view the creation of a chair of the history of medicine and surgery.

In fact, the long eclipse of the teaching of medical history had been merely official, thanks to the extramural lectures given by Dezeimeris, librarian of the Faculty, and author of the *Dictionnaire historique de la médecine* (Paris, 1828-39) and *Lettres sur l'histoire de la médecine et sur la nécessité de l'enseignement de cette histoire* (Paris, 1838), and later by Charles-Victor Daremberg at the Collège de France from 1846 to 1864, and by Professor Eugène Bouchut at the École Pratique.

Dr. Cuesco, the scholar and scientist, whom the endower of the new chair had nominated as its first occupant, declined the offer, and the Faculty was therefore free to choose between two candidates, both ex-librarians of the Académie de Médecine. The one, Guardia, had published a number of studies on the history of medicine, but his articles, which were stamped with a certain independence and bitterness of tone, had made him many enemies. The other, Charles-Victor Daremberg, associate member of the Académie de Médecine, and librarian of the Bibliothèque Mazarine for more than 20 years, had recently published his *Histoire des sciences médicales* (Paris, 1870).

As a result of a unanimous vote of the Council of the Faculty, Daremberg was appointed, on 2 May 1870, to the new Chair of the History of Medicine. It was a just tribute to the work of immense scholarship devoted to the ancient masters of medicine by the translator of Hippocrates and Galen.

Earlier Years

Born in Dijon on 17 April 1817, of an apparently humble family, the young Charles-Victor had, in the first place, to undertake intensive literary studies in his native town, under the direction of a priest, who later became Mgr. Morlot, Bishop of Orleans. He chose as his career medicine, in which he could combine his cultural studies with scientific practice. After acting as house physician in the Dijon hospital, he came to Paris in 1836 and for 8 years zealously walked the hospitals and attended lectures under Cloquet, Piorry, Andral, Lisfranc, Michon, Velpeau, Bouillard,

Ricord and Cazenave, his chosen teachers. For 3 consecutive years he devoted himself, in the capacity of special assistant to Blainville and Gratiolet, to anatomical studies in the theatres of the Muséum d'Histoire Naturelle so as to verify, scalpel and greek text in hand, the work of dissection of the physician of Pergamos, and, like Cuvier, Camper and Blainville, he arrived at the conclusion that Galen had operated only on monkeys and other animals.

Professor Laboulbène has pointed out that Daremberg's first medico-literary work was a volume of 64 pages entitled *Bon jour, bon an.* This bears on the title page the words " Mon premier ouvrage," and then, " Premier livre que j'ai fait " as well as his signature. It is an almanac for the year 1839, with wood engravings, and was published at Auxonne by X. T. Saunié, printer and bookseller. In it are to be found astronomical tables and rules of health and practical medicine.

On the 20 August 1841, Daremberg submitted as his thesis for the degree of doctor of medicine, *Exposition des connaissances de Galien sur l'anatomie, la physiologie et la pathologie du système nerveux* (Paris, De Rignoux, 1841, 96 pp.). Dedicated to Drs. Guéniard and Descuret, who guided his early steps in medicine, it is a stirring tribute to Galen's system, and to its applications in diseases of the nervous system. The thesis was the fruit of reading entire treatises, and of research on the origins of Galen's knowledge in the work of his predecessors and on the fate of that knowledge in the works of his successors. Daremberg concludes in these terms:

> " Combien ce puissant génie aurait dû hâter le perfectionnement de la science, s'il avait su mettre un frein à son imagination, s'il ne s'était pas laissé emporter comme un cheval indompté par son goût pour les systèmes et les explications, et surtout si ses successeurs n'avaient pas négligé le côté vraiment pratique de ses volumineux ouvrages pour s'égarer avec lui à la poursuite de théories surannées ! "

From 1842 to 1849 Daremberg was medical officer to the Bureau de Bienfaisance and medical inspector of the primary schools of the Quartier St-Jacques in Paris, but during this time he continued to pursue his studies of greek, latin and french texts and manuscripts. In 1843 he published a translation of selected works of Hippocrates, *Œuvres choisies d'Hippocrate*, of which the second edition, published in Paris in 1855, includes commentaries and notes and is preceded by a general introduction.

Medico-historical Tours

It was at this point that this great traveller and scholarly interpreter of the ancient masters of medicine set out on the first of a series of tours abroad, which, sometimes on an official mission, sometimes at his own expense, he was to make, over a period of nearly 10 years, with the object of studying, analyzing, extracting or collating greek and french manuscripts dealing with the medical sciences, and of delving into scientific libraries. Four times he toured Italy and Germany and twice he went to Switzerland and Belgium. In the course of eight journeys to Britain, this indefatigable traveller visited London, Oxford, Cambridge, Edinburgh, and the Ashburnham and Sir Thomas Phillipps libraries.

After two years of preparatory studies, Daremberg was sent in December 1844, by the Minister of Education, Willemin, on a medico-literary mission to Germany for three months. There he examined the papers of Professor Dietz, the eminent hellenist of Koenigsberg, who died in 1836, and he returned from this tour with important documents concerning Hippocrates, Rufus of Ephesus, Oribasius, Galen and the School of Salerno; in his report to the Minister (Paris, 15 April 1845) he gives a very interesting account of his mission. After this first journey he published the *Traité sur le pouls attribué à Rufus d'Ephèse, publié pour la première fois en grec et en français, avec une introduction et des notes* (Paris, 1846), as well as various articles, notably translations of two works by J. Rosenbaum on " The history and critical analysis of doctrines on diseases of the skin " and " The history of syphilis in ancient times, Part I ", in Cazenave's *Annales des maladies de la peau et de la syphilis* (Paris, 1844-1852).

Librarian to the Académie de Médecine

When, in 1846, the post of librarian to the Académie de Médecine became vacant, Daremberg applied for it and was appointed. He held this post until 1849 when, as the result of a difference with the administration, he left the Rue de Poitiers to join the Bibliothèque Mazarine. His articles on medical scholarship, history and criticism in the *Gazette médicale* and in the *Union médicale* attracted public attention during the same year.

Meanwhile, the voice of the Congrès Médical made itself heard, and during the course of this same year, Daremberg was asked to give an additional course on the history and literature of the medical sciences, the first lecture being published in the *Union médicale* in 1847. A souvenir of this course, which was interrupted by the political events of 1848, is, however, left to us in the *Essai sur la détermination et les caractères des périodes de l'histoire de la médecine* (Paris, 1850), which consists of fragments of the course first published in 1848 in the *Gazette médicale*. These lectures were not to be resumed until 1864.

Meanwhile, Daremberg continued to publish his work. In 1847 there appeared a description of and extracts from manuscript no. 2237 in the Bibliothèque Royale, Paris: *Aurelius. De acutis passionibus*, the text of which was published for the first time from a manuscript in the Bibliothèque de Bourgogne in Brussels (Breslau & Paris, 1847). A year later we have *Fragments du commentaire de Galien sur le Timée de Platon*, published for the first time in greek and french (Paris, 1848). At the same time, accounts of his travels formed the subject of several articles, notably one on " A short account of a medico-literary tour in England ", which appeared in the *Gazette médicale* (4 November 1848), and in which he announced plans for a library of greek and latin medical writers (prospectus published by V. Masson, Paris, 1847, 69 pp.). As bibliographer he edited a *Catalogue raisonné et analytique de tous les manuscrits grecs médicaux et des plus importants parmi les manuscrits latins et français de Paris et des Départements.* He included the greater part of his work either in official reports inserted in the *Journal général de l'instruction publique*, or in the *Notices et extraits des manuscrits médicaux . . . des principales bibliothèques d'Europe. 1° Partie: Manuscrits grecs d'Angleterre* (Paris, 1853), or else in various editions of greek or latin texts, or in the *Collectio salernitana* . . . published in Naples by Henschel, Daremberg and Renzi.

Bibliothèque Mazarine

It was on his return from a tour of investigation in Italy with Renan in 1849, during which he visited the Vatican, Florence, Siena and the Abbey of Monte Cassino, that he had to leave the Académie de Médecine and join the Quai de Conti library. He remained there up to the time of his death in 1872, and it was from there that he published, in the course of 23 years, his principal works.

In collaboration with the dutch scientist Bussemaker of Amsterdam, on whom he commented in his report to the Minister on his return from his first tour in 1845, as being " trop occupé de Galien pour songer à Oribase", he started in 1851 to publish the greek text with a french translation of *Œuvres d'Oribase* (Paris, 1851-1876, 6 vol.), which was completed by A. Molinier.

It is not possible within the scope of this article to review all the works of so prolific an author. We can only mention the principal ones amongst those prepared either in the calm atmosphere of the Bibliothèque Mazarine or in the shade of the forest of St. Germain on the small country estate at Mesnil-le-Roi, where from 1840 onwards Daremberg liked to spend the summer months; there, with his great friend Littré, he divided his time between his studies and a country clinic, where the two physician-philologists gave their services to the poor of the neighbourhood. It was also in this quiet retreat that this expert bibliophil formed the fine library on ancient medicine of more than 12,000 volumes, which the Académie de Médecine was to acquire in 1873 from his widow.

We shall mention, however, the *Glossulae quatuor magistrorum super chirurgiam Rogerii et Rolandi* (Naples, 1854); *Œuvres anatomiques, physiologiques et médicales de Galien*, translated for the first time into french, with notes (Paris, 1854-56, 2 vol.); *A. Cornelii Celsi de medicina libri octo. Ad fidem optimorum librorum denuo recensuit, adnotatione critica indicibusque instruxit* (*Leipzig*, 1859); *Gymnastique de Philostrate*, with french translation and notes (Paris, 1858); *La médecine, histoire et doctrines*, 2nd edition (Paris, 1865); *La médecine dans Homère ou études d'archéologie sur les médecins, l'anatomie, la physiologie, la chirurgie et la médecine dans les poëmes homériques* (Paris, 1865); *État de la médecine entre Homère et Hippocrate: anatomie, physiologie, pathologie, médecine militaire, histoire des écoles médicales* (Paris, 1869); *Recherches sur l'état de la médecine durant la période primitive de l'histoire des Indous* (Paris, 1867); *Œuvres de Rufus d'Ephèse* (Paris, 1879).

Daremberg did not confine his work to the history of medicine. He contributed to the *Journal des savants* and was also chosen as scientific correspondent to the *Journal des débats*, in which he published numerous articles on history and philosophy. He was also one of the editors of Franck's *Dictionnaire des sciences philosophiques* (1844-52, 6 vol.) (art. Galien) and of Dechambre's *Dictionnaire encyclopédique des sciences médicales* (Paris, 1869-73).

In 1864 the Minister of Education asked Daremberg for the second time to deliver a course of lectures on the history of the medical sciences to the Collège de France. The 175 lectures that he read between 1864 and 1867 provided the material for his *Histoire des sciences médicales, comprenant l'anatomie, la physiologie, la médecine, la chirurgie et les doctrines de pathologie générale* (Paris, 1870, 2 vol.). In spite of its title and size, this is a fragmentary and rather unequal work, because of the requirements imposed by the publisher Baillière; none the less, it remains to this day one of the best-documented histories.

The Académie de Médecine, of which he had been honorary librarian since 1849, elected him, on 11 March 1868, as a *membre libre*. At the instance of his friends Littré and Sylvestre de Sacy, Daremberg had, in fact, already agreed to put forward his candidature for the seat left vacant by the death of Montagne in 1866. His brilliantly successful election by 50 votes to 20 for Th. Roussel and 6 for Amédée Latour was not merely a just recompense but also a tribute to a learned physician.

Professor of the History of Medicine

The war of 1870-71; the siege of Paris, during which Daremberg spent his days at the field-hospital organized by Paul Broca; the Commune which forced him, under threat of arresting both him and his son, to leave Paris suddenly on the 10 April 1871—all these things prevented him from beginning his course of lectures and from responding immediately to the summons of the Faculty. The cardiac disease to which he had been subject for some time further delayed the preparation of his course after his return to Paris on the 21 May. The first lecture could not take place until the 11 November 1871. Even then it was shortened on account of the state of fatigue of the Professor who was short of breath and obviously ill. The lecture dealt with the " démonstration historique de la supériorité des méthodes d'observation et expérimentale sur les méthodes *a priori* " (Paris, 1871), and demonstrated, in perhaps too-learned a form for an inexpert audience, the importance of medical history.

Reduced in health as he was, this great historian was not perhaps able to make understood and appreciated all the advantages of a course, the original plan and method of which he had no time to modify. The *Dictionnaire des antiquités grecques et romaines*, the editing of which he had undertaken in collaboration with Saglio, still remained to be published, and during periods of remission from his illness, he did not lose hope of ensuring its publication. If he was not able to see this monument of scholarship, which was to run to 8 volumes (Paris, 1873), completely printed, at least he had the joy of reading the first sheets a few hours before his death.

Daremberg died on the 24 October, 1872 at the age of 55, in his peaceful home at Mesnil-le-Roi. This great historian of ancient medicine, who was as modest as he was hard-working, would not have desired obituary speeches. His monumental labour is the best possible memorial of the work of a universally respected scientist and scholar.

* * *

Dr. RIDES' principal medical interests have been in paediatrics, especially in its preventive aspects. She has also had a special interest in Czechoslovakia and its health problems, and in April 1946 she was appointed to the staff of the British Council in Prague as Medical Adviser

MEDICINE IN CZECHOSLOVAKIA

Impressions of an English Observer

Dr. ARNA E. RIDES

Although many are familiar with the names of Purkinje, Mendel, Skoda, Rokitansky, Bednar, Chvostek, Jesensky and Edward Albert, few of us realize that these great men were Czechs or Slovaks.

Before the 1914–18 war, Czechoslovakia was a part of the Austro-Hungarian Empire and the great czech and slovak physicians often worked in Austria and Germany. They therefore, came to be regarded as Austrians. It was not until 1882, when the Medical Faculty of the ancient university of Prague (founded in 1348), was divided into czech and german schools, that an independent school of czech medicine was recognized, and only after the liberation of the Czechs and Slovaks in 1918 was this national school of medicine able to develop freely.

The rate of development was rapid. Medical schools were founded in Brno and Bratislava, and soon achieved reputations outside the borders of the State. Many fine buildings stand as a memorial to the excellent work done in this period. I would mention particularly the fine Purkinje Institute in Prague, which houses the university departments of histology, pharmacology, and general biology ; and the splendid Masaryk Homes at Krc, near Prague, built by the city for the aged, the incurable, and for children suffering from chronic disease or congenital abnormalities. The names of men like Pelner, Hlava, Mares and Kukula became known throughout Europe.

However, during the period between the two wars the influence of germanic medical thought remained. The german medical school in Prague had a distinct advantage over the adjoining czech school, in that it was able to exchange its teachers with those from the great austrian and german centres. The czech school, on the other hand, was poorer in equipment and without the same opportunities for external contact. During this time, french medicine ranked next to german in its influence over czech medical thought. The french universities encouraged visits by czechoslovak doctors and students, and many great Frenchmen paid visits to Czechoslovakia. The fine work of the French Institute in Prague was a major factor in fostering this close friendship. After 1920, the influence of american medicine gradually increased. Young doctors, who are now professors and university teachers, went to study in America with the aid of Rockefeller Fellowships, and many of the finest health institutions in the Republic were built with the aid of Rockefeller funds, for example, the beautiful State Hospital in Kosice (fig. 1), the State Health Institute and the Masaryk School for Social Workers in Prague. American journals began to appear in the university departments and clinics, and English began to be studied to a greater degree. English medicine, too, began to exert an influence on czech medical thought. A number of doctors came to study in Britain. Some of these, Professors Pelc and Simer, for example, lost their lives at the hands of the Germans. Others such as Professors Prusik, Sumbal, Syllaba and Wolf have based their teaching on the experience gained in Britain.

But even to-day, in spite of the consequences of the war, the predominating influence of german medical thought remains. It is most encouraging, however, to see how profoundly conscious the czechoslovak medical profession is of this fact, and how diligently it seeks to widen the foundation of its science, and to base its medical thought on our common international scientific heritage.

Medicine during the Occupation

Medicine in Czechoslovakia suffered severely as a result of the war and the occupation. The profession was isolated except from Germany, just at a time when medicine in the rest of the world was advancing with incredible rapidity. Many of the best men were imprisoned, sent to concentration-camps, or killed. 61 university teachers in Prague and Brno were killed or died as the result of ill-treatment, and a further 49 were arrested and imprisoned in concentration-camps but survived. The universities in Bohemia and Moravia were closed and the professors placed on retirement with a small pension. The university teaching hospitals were converted into ordinary hospitals and forbidden to pursue scientific work. The junior doctors were sent to work either in the country areas or to Germany. For six years no students were taught, and postgraduate teaching was difficult.

Fortunately, few hospitals were completely destroyed by war or air-raids, and new hospitals were even built or completed—the Praha-Motol, originally built as a military hospital, and Vysne Hagy, the beautiful sanatorium in the Tatra ; the hospital (now the clinic of Professor Prusik) was greatly improved. Some hospitals were fortunate in acquiring new *x*-ray plants and sterilizing equipment, which the Germans installed but had not time to remove. On the other hand, a great deal of the more delicate equipment was stolen. The university theoretical departments were much less fortunate than the hospitals. They were converted to other uses, the buildings mutilated, the delicate laboratory apparatus broken, the microscopes stolen and the books lost. Although Slovakia remained an " independent " state, treated " favourably " by the Germans, and the University of Bratislava was allowed to remain open, numerous teachers were removed from their posts, and medicine was just as isolated as it was in the Protectorate. The hospitals in the eastern tip of the country came under the rule of the Hungarians, and much of their equipment was lost in consequence.

At the end of the war, the teachers who were left alive returned, much older, but with their spirit unbroken and determined to re-open the schools. They had to start from

the beginning to put their departments in order ; to find lost equipment, for there was no hope of obtaining new ; to repair buildings suffering from six years of neglect, or from air-raid damage ; and to reconvert those put to other uses by the Germans. They set to work with amazing speed. In Prague, lectures recommenced within three weeks of the liberation, although all the theoretical departments were left in complete disorder. The doctors and the staff joined the workmen in forming brigades to carry out the repairs. All the hospital teaching units have been open already for at least a year. It is stimulating to walk through hospitals to find medical work being carried on alongside that of builders and plasterers. Museum collections suffered perhaps more than anything else. Professor Neuman's famous and beautiful pathology museum in Brno was completely dismantled, the catalogues destroyed and many specimens broken. It will take years before it is in order again. But this is only one example. In Prague, nearly all the good collections have been lost or ruined.

Present Difficulties

As a result of the occupation, a number of very serious difficulties are now facing the profession. First, there is a very considerable decrease in the number of doctors—from 10,000 before the war to less than 7,000 at the end of the war, many of whom were already past retiring-age. Moreover, during the war-years, doctors who would normally spend two years in a university clinic (i.e., hospital teaching-unit) and then become general practitioners, were forced to remain in the hospitals. As a result, there are now too many clinical specialists and too few general practitioners. Even more important, however, is the lack of trained men in the theoretical and scientific branches because, during the occupation, all scientific research work was strictly forbidden, although work was carried on to a small extent in secret. The lack of trained research workers is felt in all branches of medicine and is the most important feature of medicine in Czechoslovakia to-day, explaining why so little research work is being carried out in the Republic.

There is a great shortage of literature, and practically the only textbooks available are german, although czech books are being published and reprinted as fast as possible. Students have to delay taking examinations until they can get a textbook to use. The thirst for literature from abroad is tremendous, but unfortunately the supply is still very limited.

The training of students presents great difficulties. Since the universities were closed during the war, doctors have to be trained to make up for six lost years. The numbers required were considerably overestimated immediately after the liberation, and all young people wishing to study medicine were admitted. Last year 5,620 medical students were enrolled at Prague University alone, as compared with 2,829 before the war (together with an additional 1,000 at the German University, now closed). There were 2,586 in the first year alone, and classes had to be given in the biggest hall in Prague with the aid of microphones. The teaching staff had to be increased from the 1937 total of 100 to 540. Fortunately many of these students had only a short period of study to complete their training, and over 1,000 qualified last year.

This situation caused intolerable strain to teachers and students alike. The medical teachers are profoundly conscious of the unsatisfactory position at present, and are doing their utmost to overcome the difficulties. It is evident that some solution must be found to correlate the number of students both with the number of doctors required and with the teaching-facilities of the medical schools.

Medical teaching has always followed the austrian pattern in taking place almost entirely in the lecture-room. Clinical training is allowed, but is not compulsory except for very short periods, and the relation between student and professor is much more distant than it is in Britain. However, one hears discussion on all sides about reform of the medical curriculum, and great interest is taken in teaching-methods abroad, particularly those in Britain.

In an attempt to deal with the great influx of students, and also to decentralize medicine by establishing important hospital centres outside the main towns, three new medical colleges were opened at Plzen, Hradec Kralove and Olomouc. These schools started without buildings, equipment, or books within 6 months of the liberation. The hospitals in the three towns were upgraded to university clinics, and a start was made in establishing theoretical departments. The work has already gone ahead rapidly. When I was in Plzen in the summer, a fine building was being converted into a theoretical school for use in the autumn, although it was known that very little equipment was likely to be available for years to come. At this time Plzen had no medical library. Olomouc is building new " utility " departments in the grounds of the hospital. A new and completely adequate " utility " anatomy department is already in use. Here, again, there is a great shortage of equipment, although a library has just been started with about 40 books. I was most interested to hear that the bedside method is being employed in teaching clinical medicine. A military academy has been converted into a medical school in Hradec Kralove, and here the school has been fortunate enough to inherit a fine international library left by the german army. Professor Smetanka, the Dean, is now the proud possessor of 12 microscopes for his students.

Such are the difficulties confronting the teachers of medicine in Czechoslovakia, and such is the spirit in which they are being overcome.

Effect of the War on Public Health

The war has left marked effects on the health of the population. Food was short, especially fats and proteins, particularly in the later years. Milk was not available except for the Germans, distribution of all foods was unequal, and the development of a blackmarket a patriotic duty. Since the war, the food situation has improved with remarkable rapidity, thanks to UNRRA, an excellent harvest, and efficient distribution. Now the diet in Czechoslovakia is considerably more interesting than in Britain, although fats and dried milk are still not available in sufficient quantities to meet the needs of the children. However, the price of essential foodstuffs is higher than in Britain, and wages are lower, so that the poor mother with numerous children cannot afford to buy all the rations. The Government fully appreciates these difficulties and prices are falling steadily, although slowly. As may be expected, the poor nutrition during the war has left its marks on the children. In a survey of Prague schoolchildren conducted in 1945 and early 1946 at the request of the Czechoslovak Ministry of Health, Dr. Lewit, former assistant Medical Officer of Health of Wallasey, found 22 % suffering from evidence of malnutrition according to british standards.

One of the most alarming facts about the health situation is the extremely high infant-mortality rate. In 1944, the last year for which complete figures are available, it was 99.7 per 1,000 live-births in Bohemia and Moravia, as compared with 45.4 for the same year in England and Wales. This figure rose to 110 in 1945. In Slovakia, no figures are available after 1942, in which year it was 159. It is most unlikely that it is lower now. The neonatal-death rate in 1944 in Bohemia and Moravia was 42 per 1,000 live-births, as compared with 24.4 in England and Wales. There is a large number of factors which contribute to these high figures —to cite a few: the low standard of nutrition of the mothers; the low standard of training, the bad distribution and the inadequate supervision of midwives, and the failure to eliminate untrained women; great overcrowding in the homes (one person per room is the upper legal limit for accommodation in Prague); great overcrowding and lack of nurses in the maternity homes; poor development of the infant-welfare service; ignorance of infant hygiene, particularly in the villages (the level of health and hygiene in Eastern Slovakia always has been particularly low); decrease in the number of mothers able to breast-feed; absence of health-visitors; the overclothing of infants which leads to pyodermal infections; the gross contamination of fresh milk and lack of dried milk; and, the lack of any real co-ordination between the various branches of welfare work.

Infectious diseases increased during the war, as they did in all european countries, the increase being particularly marked in the case of diphtheria and tuberculosis. It is interesting to note that in Slovakia, where diphtheria immunization was made compulsory during the war, the incidence has steadily decreased.

The incidence of tuberculosis has always been high in Czechoslovakia. In 1935, as many people died there of tuberculosis with a population of 15 millions as died in England and Wales, with a population of 40,600,000. Naturally, the war, with its accompanying malnutrition and overcrowding, caused a further increase, as also did the fact that tuberculosis was not recognized by the Germans as a disease requiring rest, and open cases were forced to continue work in the factories. The official death-rate per 100,000 inhabitants in 1944 was 150 as compared with 62.7 in England and Wales. It is universally recognized that these figures unfortunately understate the truth. It is estimated that there are 40,000 cases in Prague alone.

Previous efforts to control tuberculosis have been hindered by insufficient sanatorium beds and lack of adequate state financial help for the patient. As a result, the average stay of a patient in a sanatorium is only 3 months. Moreover, there is no adequate system of aftercare, and few tuberculosis health-visitors, so that the relapse rate is unduly high. Moreover, the service suffers from a lack of co-ordination in all its branches.

At the end of the war, there was a sharp epidemic (5,000 cases) of typhus in the concentration-camp at Teresin, but fortunately this was stamped out before spreading amongst the general population.

It is interesting to note that, in spite of the oppressive influence of the german occupation, the incidence of mental disease did not increase during the war. After the liberation, however, there was a sharp rise in the incidence of these diseases.

Hospital Work

Many hospital buildings in Czechoslovakia are excellent—in fact, much better than the average building in Britain. In all hospitals, new and old, the wards are much smaller than in Britain, and the atmosphere is more friendly, although this is often at the expense of efficient nursing. Many hospitals were built during the First Republic. The Prague City Hospital in Bulovka is particularly fine, situated in the outskirts of the town, with each department in a separate building in extensive grounds. The chest department of Professor Skladal is excellent, and especially interesting is the infectious diseases department of Professor Prochazka (fig. 2). No suggestion ever made for the prevention of cross-infection by structural means has been omitted from this building. The Cancer Institute under Professor Moravek in Brno (fig. 3, 4) is most impressive, and so is the State Hospital at Kosice (fig. 1). The Tatra sanatoria leave one amazed by their splendour, and many of the hospitals of the smaller towns, such as Usti and Labem, have excellent buildings, although some are not large enough for present needs. The older university hospitals were built many years ago, and often leave much to be desired in their construction. The

FIG. 1

The State Hospital, Kosice

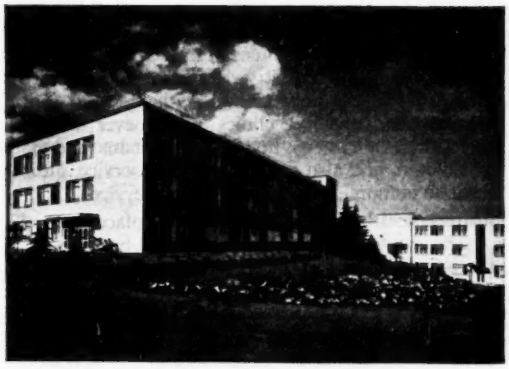
FIG. 2

Prague City Hospital, Bulovka. Infectious Diseases Department

Prague University Hospital was built originally as a monastery in the time of Maria Theresa. In spite of this, many of the departments have been altered to make them adequate, and fine new buildings have been added, although the staff longs for the time when a completely new hospital will be built. The hospital at Olomouc is old and very small, particularly now that it has been converted into clinics. Some of the clinics in Bratislava, too, are housed in poor buildings.

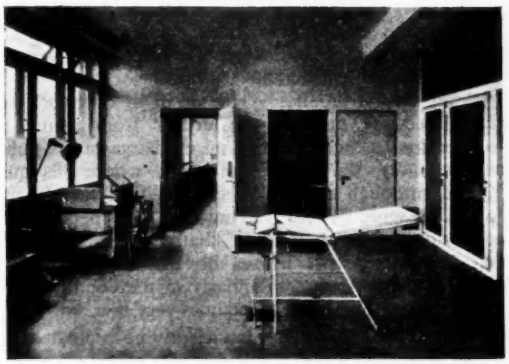
The standard of diagnostic medicine in czechoslovak hospitals is high, and only a few of the newest diagnostic methods are not yet available, e.g. bronchoscopic biopsy in cases of lung tumour. The high standard is in evidence everywhere, and I would mention, because I know them best, the clinics of Professors Charvat, Prusik, Hynek, Netousek, Syllaba, Henner, Vancura, and Podlaha, but one could continue the list indefinitely. The standard of pure pathology is very high, and I would cite particularly the work of Professor Sikl in Prague. On the other hand, the general level of treatment does not reach quite the same high standard. This arises largely from the fact that treatment has advanced relatively more rapidly than diagnosis during the war, and many new ideas involve a complete re-orientation of medical outlook, large-scale re-organization and expense and the closest co-operation between all institutions associated with health-work. This co-ordination is poor in Czechoslovakia. Even within the boundaries of one hospital, each clinic or department is a self-contained unit, much more isolated from other departments than in a british hospital. This retards, particularly, the development of such a branch as rehabilitation. Therapeutics is at the stage where disease is treated, but no attempt is made to treat the patient as a whole, particularly with the aim of re-establishing full health, by active convalescence culminating in an early return to employment. Very few hospitals have convalescent departments.

FIG. 3



Cancer Institute, Brno. General View

FIG. 4



Cancer Institute, Brno. Radium Therapy Department

Penicillin is distributed as in Britain, and excellent use is made of it. Sulphonamides, on the other hand, are used in smaller doses than those recommended in Britain and USA. This is largely because more-toxic compounds were used previously, and many doctors had unfortunate experiences with them which they do not easily forget.

Czechoslovakia is very fortunate in possessing many natural resources in the nature of springs, wells and waters, around which beautiful spas were built. Karlovy Vary (Karlsbad) and Marianske Lazne (Marienbad) are now among the finest holiday centres in Europe. However, these possessions are not without their disadvantages, notably in tending to create an unbalanced sense of values in assessing relative merits in therapeutics.

Surgical technique is excellent, but modern surgery is handicapped by three important factors. In the first place there is a complete absence of modern inhalation-anaesthesia. Wherever possible, local or spinal anaesthesia is used. Where a general anaesthetic is essential it is given by a nurse, using open ether. The surgeons are very conscious of this handicap, in particular Professor Jirasek of Prague, Professor Podlaha of Brno, Professor Rapant of Olomouc and Professor Carsky of Bratislava. Professor Jirasek has just sent an assistant to study anaesthetics at Oxford. Surgery is also handicapped by lack of specialization. Each surgeon is forced to be a general surgeon, and can spend only the time he has left over in working at his own speciality. However, here again much has already been done. Urology and orthopaedics have already long been recognized as separate departments, although fractures are still treated by the general surgeon. Other branches are rapidly developing. The world-famous plastic clinic of Professor Burian at Vinohrady Hospital, Prague, has been followed by the opening of plastic units in Bratislava and Plzen. Professor Divis in Prague is mainly interested in thoracic surgery, and the Government plans to encourage the development of this speciality by opening hospitals for the surgical treatment of tuberculosis. Departments of traumatic surgery already exist in Brno and Zlin.

The third great difficulty facing the surgeons, as indeed all hospital workers, is the shortage of nurses. This makes adequate nursing of the patients impossible, and particularly hinders good pre- and post-operative care.

Nurses

In 1937 there were 9,600 nurses in Czechoslovakia, 2,300 of whom were trained and 7,300 untrained (i.e. comparable to assistant nurses in Britain). Now there are only 7,050 nurses, 2,300 of whom are trained and 4,750 untrained. At least 2,500 nurses are needed immediately and 15,000 will be needed to man the planned extension of health services.

The shortage of nurses arises from a number of factors. Before the war the value of a trained nurse was not so well understood as it is to-day, there was a great shortage of training schools, and the social status of a nurse was far lower than in Britain. Moreover, during the war, many girls who wished to be students, particularly medical students, took shelter in the nursing schools to save themselves from being sent away in forced-labour squads. These girls have now entered their chosen professions, and are consequently lost to nursing. The nurses' training schools are good. Nurses are regarded as students in Czechoslovakia, and live in a residential school where they receive theoretical training. Arrangements are made with local hospitals for practical training in specially reserved wards. The course lasts two years, and the nurse obtains a diploma at the end of this time. Although the training is good, it is often carried out under the most difficult conditions. The oldest training school is the State School in Prague, founded after the 1914-18 war by the American Red Cross. This school is excellent, but the buildings are so inadequate that one wonders how any girl is content to live in them. The school consists of 4 converted old houses, with dark rooms and long winding corridors. Five girls have to sleep in a room large enough for two, and two lavatories serve 60 girls. British nurses must admire these girls who are willing to suffer such discomfort to train in their chosen profession. However, a new building is already standing, and the nurses wait with great impatience the day when it will be ready for them to move in.

Before the war there were 8 such schools in Czechoslovakia, and 4 more were founded during the occupation. Since the liberation, no less than 12 new schools have already been founded, a great tribute to the determination and energies of the leaders of the profession. It is planned to establish 6 more in the next two years.

The profession is, in fact, led by a band of excellent women, with wide experience outside their own country. Success in the future lies in the further extension of the number of training schools to meet the increasing demand for nurses ; in plans to give a theoretical training to untrained nurses now doing valiant work in the hospitals, and in raising the social status, living conditions, and conditions of service, of the hospital nurse. Although things look bad at the moment, I have every confidence in the future.

Social Services

As early as 1926, a comprehensive state health-insurance was introduced into Czechoslovakia, including all types of employees and their families. Farmers, shopkeepers, and professional workers, who are not employees, are, however, excluded. Unfortunately, the system of insurance is very complicated, and it is difficult to give an overall picture which is in anyway accurate. There are many small state insurance companies, according to the type of work of the contributor, e.g. manual worker, clerk, post-office employee, etc. Each company has slightly different rates of contribution and benefit. However, the work of the companies is adequately co-ordinated.

The employee's contribution amounts to about 5% of his income, and the employer pays a similar amount. There is no state contribution unless the state is the employer. The benefits include sick-pay from the 4th day of illness. The amount is reckoned as a percentage of wages, the lowest-paid workers getting 100% and the highest-paid only 50% of their earnings. The benefits also include free hospital treatment and convalescent treatment, free specialist consultation, drugs, appliances, spectacles and dentures ; maternity benefit, burial benefit and old-age pensions. The insured person is able to choose his own doctor from the insurance list, providing the doctor is willing and able to accept him as a patient. In many areas, the insurance doctors work in centres, where also the specialists employed by the insurance companies hold their consultations.

Doctors are paid according to the number of sick insured persons consulting them per quarter. The quarterly fee is equivalent to 3 shillings per sick head. In addition to this, doctors receive payment for special treatment, e.g. dressings, injections.

The workers are also insured against accidents. The insurance includes accidents occurring during the journey to and from work. The benefits for permanent disability are paid monthly, and calculated according to a complicated scale of degree of disablement and original earnings. The contribution is paid by the employer.

Many of the other aspects of social service are not so well developed as they are in Britain. There is a large number of infant-welfare clinics, especially in the towns, but still too few in the country districts. These clinics are well attended and are appreciated by the people. On the other hand the antenatal clinics have never been very popular. There are many homes for orphans and handicapped children, and also a school medical service, although this is not so comprehensive as the british service.

Industrial health holds an important place in welfare work. The newer factories are all well-built from the hygienic point of view, with good ventilation, and adequate washing and cloakroom accommodation. Factory canteens are rapidly being established in all the bigger works. However, the guarding of machinery is not so adequate as in Britain, and the accident rate is higher. This matter is receiving close attention, and a big drive is being made, both by education and increased guarding, to decrease the number of accidents.

There are three big handicaps to welfare work. In the first place, it is unfortunate that doctors employed in public work, and also those employed in research, are paid very low salaries, and usually work on a part-time basis. This means that most of these doctors are forced to overwork themselves grossly by holding two posts at once, or by undertaking private practice. The strain of overwork and financial insecurity prevents the doctor from giving his whole attention to the planning and discharge of his public duties. Secondly, the number of social workers is quite inadequate, although they are well trained at the Masaryk School in Prague. There is, however, no person who undertakes quite the same work as that of the british health-visitor. Further, district nurses do not exist, leaving a great gap in the services, particularly in the country areas, where the level of hygiene is sometimes very low.

Finally, the services are not sufficiently co-ordinated and integrated with the general health-services of the country.

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PROFESSOR CHARLES McNEIL was the first occupant of the Edward Clark chair of Child Life and Health in the university of Edinburgh, a post which he held for fifteen years until his retirement last year
His article contains personal views on some controversial subjects but, coming from such a source, they should command general interest and attention

CARE OF CHILDREN

A Critical Review of the "Curtis Report"

Prof. CHARLES McNEIL

The report[1] of the Care of Children Committee published last September deals with a subject of great importance, in which public interest had already been aroused by cases of cruelty to boarded-out children, and in particular by the shocking details of a particular case. The Committee appointed by three Ministers of State in March 1945, under the Chairmanship of Miss Myra Curtis, had as its task—

> "to inquire into existing methods of providing for children who from loss of parents or from any cause whatever are deprived of a normal home life with their own parents or relatives; and to consider what further measures should be taken to ensure that these children are brought up under conditions best calculated to compensate them for the lack of parental care."

This is a wide and complicated field of inquiry, and the Report fully reflects this complexity, as well as the painstaking labours of the Committee in bringing the inquiry to completion in eighteen months.

Law, Administration and Statistics

The first part gives an outline of the four[2] statutes that govern the care of homeless children in England and Wales, and of the administrative structure that has been set up to enact and control the provisions of these statutes. At the centre in Whitehall, the Home Office, the Ministries of Health, of Education and of Pensions, and the Board of Control all have a share in direction, with their local representatives and authorities in the Boroughs and County Boroughs. The multiform pattern of administration is determined by the differing categories of homeless children, and by the gradual evolution of state agencies dealing with them, beginning with destitute children gathered into workhouses under the Elizabethan Poor Law, and ending with war orphans of George VI committed to the Ministry of

[1] [For title, particulars, and price, see *Book Reviews*]

[2] These statutes are The Poor Law Act 1930; The Children & Young Persons Acts 1933 & 1938; The Public Health Act 1936; The Adoption of Children Acts, 1926 and 1939.

MEDICINE IN CZECHOSLOVAKIA

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Future Proposals

Czechoslovakia has drawn up a Two-Year Plan to establish her economy on a sound basis. A number of important medical measures is proposed. In the first place, there is to be considerable reorganization of the health services. Health clinics, similar to the british conception of a health-centre, have already been set up in the border-regions, and they will be extended to the major towns during the next two years. Three such clinics are already functioning in Kosice.

By gradual steps, the present complicated health-insurance schemes will be unified and the remuneration of the doctor raised. The state will take over the sale of drugs, and the spas will be taken over by the state, the trade unions and the insurance companies, to allow all classes of people to benefit by their facilities.

A major campaign will be launched to combat infectious disease. Diphtheria immunization will be made compulsory for the whole nation, at present it is compulsory in the city of Prague and in Slovakia. Plans have been drawn up to combat the widespread incidence of tuberculosis. The number of beds available will be increased by 3,000, and departments of thoracic surgery will be established. Attempts will be made to isolate highly-infectious incurable patients. Three large settlements will be established, inspired by Papworth Village settlement and under the guidance of Dr. R. R. Trail. Tuberculosis patients will have their incomes incremented by the state to the essential minimum, and schoolchildren will be subjected to periodical skin-testing. The problem of the extremely high infant-mortality rate will be dealt with by establishing infant-welfare centres where they do not now exist. Ten will be established in 1947, and 10 in 1948. Children's departments will be established in all general hospitals. The methods of control, curriculum, and examination-standards of midwives will be revised. The present course of 10 months without previous nursing-training will be increased to two years.

The whole position of nurses will be revised. There is to be an increase in the number of training schools, the establishment of postgraduate diplomas, and the social level of the nurse will be raised, with reference to her pay and living conditions. Attempts will be made to attract into the profession better-educated girls, and to train the untrained nurses now serving in the hospitals.

Mental-health clinics will be established, also V.D. clinics, anti-rheumatic clinics and cancer clinics. The industrial-health services will be extended, using the experience already gained in the excellent industrial-health service at the Bata works in Zlin and elsewhere. Finally, laws will be passed to insure the clean production, preparation, and sale of food.

Czechoslovak-British Medical Relations

There has been a considerable increase of interest in british medicine since the war. After long isolation, czechoslovak doctors have a tremendous interest in work that has been done abroad, and the many czechoslovak doctors returning from Britain in the early days after the liberation brought back with them news of the medical advances during these years.

The British Council opened an office in Prague soon after the liberation. Supplies of medical and other literature were sent, and later a medical adviser was appointed to assist in establishing contact between the czechoslovak and british medical professions. The demand for british books, periodicals, and lecturers is great, and it is the ambition of many czechoslovak doctors to visit Britain sometime during the next two years. Very many are busily learning English, and attend anxiously classes in british medical terminology, run by the Council's British Institute.

Since the war a number of british doctors has visited the country, as guests either of the British Council, the Czechoslovak Government, or of medical societies. The most notable of these were Dr. R. R. Trail, Mr. G. C. Knight, Dr. J. A. Charles, Sir Philip Noel Panton and Dr. S. C. Dyke. They were warmly received and gave lectures to crowded halls. The czechoslovak doctors want to know why Britain cannot send more lecturers. They would like Britain to send a team of 12, such as came from USA for two months during the summer.

At present an Anglo-Czechoslovak Medical Society is being formed ; its inaugural meeting in Prague was called at very short notice, but no less than 110 doctors were present.

Pensions. This specialism in state and also in voluntary philanthropy, hitherto beneficent in its operation, is now a bar to further progress; and the Curtis Report recommends that the central administrative control of all deprived children, whether destitute, deserted, legally adopted, delinquent, physically or mentally defective, or orphaned should be vested in one department of central government. This single central department would draw up standards and rules and would supervise their operation by inspection and advice. This section ends with a statistical statement of the present numbers of children in England and Wales deprived of a normal home life and of their different categories. The total is 124,900: almost one half of this total is classed as destitute (57,600); of the remainder, the largest class are children removed from home by Order of Court, as delinquent, or in need of care and protection (23,400).

Survey of Institutions and Foster-Homes

The second section describes the many agencies and institutions, state and voluntary, which today attempt to meet the needs of these deprived children by providing a substitute for the home life they have lost; and which do so either by adoption, by boarding-out in selected homes, or by maintenance in institutions or children's homes. Further, it gives the result of an extensive survey by the Committee of the actual conditions in these institutions in all parts of the country and in many foster-homes where children are boarded-out. Of this survey, carried out by individuals and groups of the Committee, it is possible to give here only some of the general conclusions of the Report. Taking the institutional side, the Report states that the greater number of these community-homes were " reasonably well run from the standpoint of physical care "; while " some were very good, some indubitably bad." Where conditions were bad " the defects were not of harshness, but rather of dirt and dreariness, drabness and over-regimentation. We found no child being cruelly used in the ordinary sense . . . " But both in the detailed reports of the survey, and in the general conclusions drawn from it, the Report emphasizes the lack of personal interest and affection for the individual child shown in many Homes, and the serious effects of this on the personality of the children and especially of the older children, both in retarding the intellect and in stunting and distorting moral development.

These criticisms are applied both to voluntary and local-authority institutions. Other points of adverse comment are lack of equipment, lack of toys and playgrounds, poor accommodation, and deficiencies of the staff in personal qualities and training. There is strong criticism of the practice of keeping children in wards adjoining those of adults in old Poor-law buildings. The records of the children, apart from medical records, in nearly all institutions were very poor. The care of infants and young children under five was generally better than that of older children. Of the character of the Superintendents, Matrons and House-mothers, it is said with emphasis that " On the personality and skill of these workers depends primarily the happiness of the children in their care." Thus in paragraph 145, dealing with a nursery adjoining the wards of an adult workhouse it is noted—

> " The relationship between the Master and Matron and children approached very nearly to normal home life. The Master made toys for them, played with them and joked with them. He assured us that his Committee supported him in all his suggestions as to improvement . . . "

This paragraph immediately follows one describing another workhouse nursery with the worst conditions revealed by the survey, which has received much public quotation and notoriety.

Another example of the effect upon the children (in this case older children) of the right quality in the staff is worth quoting (p. 64)—

> " There is a very happy relationship in this Home " [a cottage Home under Public Assistance] " between the foster mother and her 14 boys. She has been in the work for a number of years and obviously understands boys and how to get on with them. At the time of my visit some were playing halma with her and others were drawing with crayons or reading. The boys go out to the local Church Scouts and are also often allowed to go out by themselves by bus or to such amusements as the neighbouring fair."

These two examples are sufficient to endorse the comment of the Report on " the much greater importance of the personality of the staff than of any system by which the services were run ". The definition of *personality* in this connexion may be given as a love of children; of this more will be said later in discussing the qualifications and training of the staff of these institutional homes for children.

Foster-Homes (Boarding-out)

In view of the O'Neill case [a notorious case of ill-treatment by foster-parents], the survey and conclusions of the Committee on the condition and well-being of children maintained for reward in the homes of foster-mothers are reassuring. Here there was little or nothing of the dullness and loneliness of spirit found in the institutional homes; " indeed the foster homes as a whole made a decidedly favourable impression." But the cautionary remark is made that the risk remains of instances of incompatibility between the foster-parents and the child, and of " acute unhappiness " in the child: and various criticisms are made of faulty and loose administration of local authorities which would allow these exceptional cases to go undetected.

Recommendations

The recommendations cover every aspect of the problem of all classes of children deprived of their homes—legislation; central and local administration; and the placing of the children in new homes by adoption, boarding-out, and group-treatment in institutional homes. Again it is possible in this review to make only a selection of these proposals, and to sum up in a final commentary.

The recommendation of a central single Ministry with suitable staff, and with powers of framing policy and supervising its execution by a special *ad hoc* committee of all local authorities has already been mentioned. All voluntary organizations and homes dealing with these children should be registered, subject to inspection by the central department, required to conform to the rules and directions of this department, but otherwise permitted to continue their present work.

Each local-authority committee should have a Children's Officer, with special experience in child care, preferably a woman, who would be responsible for the welfare of all deprived children in the area; and where necessary this Children's Officer would act for several Children's Committees in combination as a Joint Board; her appointment

should be approved by the central authority, and her annual report to the local committee and council should be sent also to the central authority; her responsibility for the children under care would be delegated to a staff of women, each of whom would maintain personal contact with a group of children.

Adoption first of all, and then boarding-out make better provision than institutional care; and the children's officers should be responsible for receiving and investigating cases, and through the assistance of trained visitors for placing the children in suitable homes. A vigorous attempt should be made to increase the boarding-out service.

In institutional homes, none should form a structural part of adult institutions managed by public assistance departments of local authorities. In the case of infants, their nurseries should be in the charge of medical specialists. In the Homes for older children, ages and sexes should be mixed, and the number in any Home should not exceed 12: the education of these groups of children should be in neighbouring primary and secondary schools. Every assistance should be given to the children in choosing their future work, and more attention should be given to the after-care of the children when they leave the residential homes.

The number of deprived children at present under public care should be increased by including adopted children, by extending the age of boarded-out children under supervision from 9 to 16 years, and by registering all children in voluntary Homes. It is calculated that these additions would bring the present total of 125,000 deprived children in England and Wales to 150,000 or 200,000.

Other recommendations deal with physically- and mentally-defective children, with approved schools and remand homes, and with emigration.

Commentary

The report is a valuable document and also an ominous social landmark. It contains a mass of important information; and both in arrangement and presentation it reflects much credit on the industry, ability and moderation of its authors. It deals with problems and issues of the widest interest and of deep national importance; and its proposals should receive thorough and also critical examination.

The problem it deals with is the mitigation of the evils that must befall children who for any reason are deprived of home and family life. The number of these children, already large, is increasing; and although the immediate question is the alleviation of their lot, the more fundamental question of the causes that lead to the breakdown of family life raised at the beginning of the Report, is admitted to be of the utmost importance, but is left aside as falling outside the terms of reference.

Foster-Parents

The success of these measures of alleviation depends above all else on the moral qualities of the new guardians of the children who assume the duties of parents. This is clearly stated in the Report and will receive universal agreement. Everyone also will agree that these foster-parents, whether in real homes, or in institutions, should be supplied with all proper facilities of accommodation, equipment, and service, necessary for child life, and should be subject to inspection and supervision in performing their duties. Many faults of this kind, in bad environment and in loose and faulty inspection, are pointed out in the Report, and can be remedied without drastic changes in the existing machinery of administration. But the best results will be attained only if the women and also the men, who are *in loco parentum* have in high degree the feelings of parents towards their children, and not only affection but also obligation, and the power to win from the children answering affection, trust and obedience. Where these qualities are present, the inspecting functions of the state ought to be unobtrusive and should leave a large measure of freedom and diversity of training methods to those in charge of the children.

Powers of Central Department

The appointment of children's officers, preferably women, throughout the country in areas of suitable size is a valuable proposal of the Report. The other proposal of a single central department determining general policy, drawing up standards and rules and with a staff of inspectors, may be logically-sound on paper but has the usual dangers of centralization—a deadening uniformity of policy and methods, and the weakening of local interest, initiative and responsibility. A graver danger is the hasty and ill-considered application of doctrinaire theories to the moral education and character-moulding of children, and their enforcement on a national scale. Thus the Report favours a more lenient discipline of children in their substitute homes and gives many examples of its views in this matter; and at the same time it places in Whitehall the right to draw up and enforce the rules for the home discipline of these children. It proposes further that all *legally-adopted children should now be subject to inspection*, and presumably to the enforcement of the central code of child-discipline and training. From this it is only a short step to state inspection and control of children in all families, when we shall have arrived at complete *étatisme* in family life.

Discipline

The training of children at home, which is discussed both in principle and in detail in the Report, is of great importance—" the child is father of the man ". The first quality in good parents is love of their children; second, but still cardinal, is proper discipline and control. In the Committee's survey of foster-homes and institutions, which was extensive and searching, no case of cruel or savage discipline was found; but while many good and acceptable proposals are made for relaxations of unduly strict routine and discipline, including the caning and birching of boys, there is no mention of the importance of discipline as a whole (p. 168). This is a regrettable omission; and especially as the increasing delinquency in children is believed to be largely due to the lack of control and discipline in their home life. In this hard and difficult world, and as the right preparation for their taking a robust part in it, the time has come for a return to a stricter code of discipline in the family life of children. And in institutional " homes " a good standard of discipline is even more important, and those in charge should be enjoined and encouraged to maintain it. Good discipline is compatible with freedom and happiness. The Report rightly insists on the primary importance of affection and affectionate personal interest in those in charge of Children's Homes, but it does not

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Dr. R. A. McCANCE is professor of experimental medicine in the university of Cambridge. He is well known for his nutritional work, and during the war he was directly engaged upon the experimental study of rationing problems

FOOD CONTROL IN BRITAIN 1939-1945

Prof. R. A. McCANCE

The task of feeding any country during a time of stress depends upon the application of established nutritional principles to the particular problems by which the community finds itself faced.

In 1939, Britain depended upon imports for more than half her food, and the experience of 1914–18 indicated that supplies were likely to become critical in the next few years. At the same time, the extensive knowledge of nutrition which was available in 1939 indicated that it was more economical to grow food for direct consumption by man than to utilize it for rearing pigs, poultry and cattle. It was also known that men, women and children required different kinds and amounts of food, and that in times of shortage each might have to be considered separately. Armed with these general principles, the Ministry of Food faced its task in 1939 and has now published a summary of its activities.[1]

Most people who live in Britain would agreed that, on the whole, the country has been well served by the Ministry of Food. At first its task was comparatively easy, for relatively few ships were being destroyed by the enemy, and most of the countries from which Britain was in the habit of drawing her food-supplies were still able to export food. In 1940, however, the fall of Denmark, Norway, Holland, Belgium and France completely altered the situation, and with the entry of Italy into the war the position became extremely grave. Nevertheless, throughout this time the stocks of food in Britain were steadily being increased by the Ministry in anticipation of difficult times ahead, and the wisdom of this step was apparent in 1942, when the accumulated stocks of food had to be drawn upon to the extent of 700,000 tons.

In order to increase the food supplies of the country, land was broken up for the production of grain and vegetables, and the pig and poultry populations were drastically reduced. The number of cows, however, was not only maintained but increased to meet the greater demands for milk brought about by the generalized issue of milk to children and its provision for invalids. It is difficult for the " ordinary consumer " of Britain to-day, rationed as he is to about 1 litre of milk per week, to realize that the milk supplies of the country as a whole have increased since 1939. The extraction-rate of wheat was raised from about 70 % to 85 %.

[1] [For title, particulars, and price, see *Book Reviews*]

CARE OF CHILDREN

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give discipline its proper place alongside the first. The best mother is she who joins with loving care a discipline which is both strict and gentle: and this should be the model for the institutional "mother". Undue severity of discipline can be detected and corrected by a proper system of inspection. Horace describes the hardy children of the old latin peasant families as " severae matris ad arbitrium"—" under the unquestioned rule of a strict mother ".

Religion

The place of religion in the institutional home-training of children is discussed in a short and colourless subsection of ten lines (paragraph 493), and is the subject of a minority reservation. And yet, all over the world and through all recorded history, religion is and has been one of the great disciplines of life. Its practical omission from the Report no doubt reflects the popular modern view that religion is beyond the grasp of the child's mind, and also the prevailing practice of that view. In the reservation (p. 183) it is stated, " From their earliest years they [the children] need the help which is found in a growing faith." This general statement is supported in the Report on Primary Education in Scotland recently published (Cmd. 6973), where modern educationists assert that the child's mind is deeply interested in the mysteries of life and is eager to receive instruction and guidance in religion. And there is Wordsworth's great Ode on *Intimations of immortality from recollections of early childhood*, which is full of the same theme. So that there is authority, both ancient and modern, as well as the vast experience of mankind, for giving religion a high place in the training of homeless children. In the Report this matter is expressed only as a wish and a hope that the staff in charge " will no doubt find means, as good parents do, of influencing the children's lives both by their teaching and their example."

Effects and Causes

The care and training of deprived children are only palliative remedies. They do not touch the disease that has produced these thousands of homeless children—the existing widespread corruption and disintegration of family life. But if proper remedies will mitigate the effects of this disease of the family, the same remedies can and will cure the disease itself and restore the health of the family. In this sickness of family life, there are many injurious causes at work. One of them is lack of family discipline. Another, and more important, is lack of religious training, which is the most comprehensive of all disciplines, and which penetrating the life of the young child from his early years will bring him to the full stature of manhood. Wordsworth has given the right formula for the health of the family—" pure religion breathing household laws."

The Report is a most important document of social study and contains many valuable proposals which should result in the better care and training of homeless children. It raises issues which go to the root of national well-being, and which require thorough examination and discussion. In this commentary three matters have been selected which the writer believes to be objectionable and to require critical discussion: the excessive powers given to a central department over the training of deprived children; the lack of positive proposals for good discipline in Children's Homes; and the perfunctory place given to religion in the training of the children.

Difficulties due to the shortage of shipping were not the only problem which faced the Ministry of Food. Owing to the manpower-shortage within the country, and, to some extent, to enemy-action, the distribution of food had to be completely reorganized. The principle of "zoning" was introduced, by which foods produced in one part of the country were allocated for consumption there, regardless of trademarks or goodwill. Retail distribution of food had to be curtailed. Milk, for instance, was delivered only once a day, and in some places not so often.

All these adjustments were made possible by an extensive system of controls. It was relatively easy to control the foods which were imported from abroad, but much more difficult to control the food produced within the country, yet it was essential to do this. It was arranged, therefore, that all food except fish and green vegetables should be sold either to the Ministry or to accredited agents. The pigs, for example, had to pass through special slaughterhouses or bacon-factories, and the eggs through packing stations. All this was made possible only by the recruitment of acknowledged experts in all the trades to be controlled, and on the whole it must be said that these people have served the Ministry well.

To prevent a sharp rise in the "cost-of-living index", upon which many wage agreements had been based, the prices of retail foods were controlled from the beginning of the war. It was, naturally, possible to hold prices steady only at the expense of the Exchequer, and a most elaborate system of price-fixing was necessary at all stages of distribution. In the first year of the war, the subsidies cost the Exchequer £13.2 million; in 1944–45 £168.4 million.

The requirements of the individual were met by a system of rationing. Meat, bacon, cheese, fats, sugar, preserves and tea were issued in fixed amounts obtainable only on the production of the specific coupons. Tinned meat and fruits, dried fruits, dried pulses, condensed milk and a number of other processed foods were sold on the "points" system. Each individual was issued with a certain number of "point" coupons per month, and all foods sold on the "point-coupon" system were rated at so many "points". This enabled the housewife to select from the foods so sold those she preferred, and it gave an over-all ration with a limited individual choice. The system was a success. In addition, special coupons were issued to each individual for the purchase of sweets; while milk, shell-eggs, oranges and one or two other foods were allocated by controlled distribution. The special requirements for children, and pregnant and lactating women, were met by the issue of special ration-books; but with bread and potatoes always unrationed, and with the special canteen-facilities which were provided in many of the industries, it was never necessary in Britain to have special cards for heavy and very heavy workers. Anyone could have a meal in a restaurant without surrendering coupons. These were very great advantages, and there is no doubt that these two freedoms contributed in no small measure to the efficiency of the country throughout the war.

Difficult as the task of Ministry of Food must have been, it would have been many times more difficult had it not been for the goodwill and co-operation of the people. The country was never overrun by the enemy, nor was there ever any real shortage of food. People may have gathered more blackberries than they did before the war, but they were never reduced, as in Holland, to eating tulip-bulbs and sugar-beet. Thanks to this and to the mentality of the british public, there was never any risk of a big black-market.

The situation in Britain was not unlike that in Switzerland. In 1939 both countries imported more than half their food. Their problems were similar and they were solved in very much the same way. Land was brought into cultivation; livestock was reduced in numbers. The extraction-rate of bread was raised, the consumption of potatoes and cereals increased, while that of fats, meat and sugar was reduced. The Swiss did not maintain their supplies of milk at their pre-war levels, and bread was rationed, but there was never a serious blackmarket. The calories per head were never so high in Switzerland as they were in Britain, and at one period in 1944–45 they fell to a level incompatible with good health.

The british people have much for which to be thankful. They have been well, if somewhat monotonously, fed throughout the greatest war in history and during times when much of the world has been facing starvation or semi-starvation. But producers and consumers alike look forward to a relaxation of those controls which they regarded as unpleasant necessities during the war. Producers wish to be free to sell to whom they will. Consumers welcome the application of nutritional principles to the feeding of their children. They wish their boys and girls to have milk in school, if it is good for them, but they want more milk for their own tea, and they want to abandon their ration-books for ever, and to buy what they want, where they want and when they want. Let us hope that these times will come soon, not only for the people of Britain, but for all the peoples of Europe and Asia who have suffered from the war.

* * *

PUBLIC HEALTH IN BRITAIN 1939–1945

Dr. A. C. STEVENSON

London School of Hygiene & Tropical Medicine

The report[1] of the Chief Medical Officer of the Ministry of Health for the years 1939–1945 is a worthy new member of a great family—the family of the reports of the principal medical officers of the central departments concerned with public health. It is in direct line of descent from those of Sir John Simon of seventy years ago, and like these ancestors will not disappear to lie and become dusty, forgotten in the basement of the reference-libraries, but rather will become much tattered by use.

Sir Wilson Jameson outlines in his introduction what is to be expected in the body of the report and indicates who is mainly responsible for the sections. He pays generous tribute to the work of the members of his own department, to his Medical Advisory Committee, and to Medical Officers of Health with the Local Authorities.

It is quite impossible in the space available here for the reviewer to do more than mention the highlights of the various sections, for there is too great a mass of information. If he can interest readers sufficiently to make them refer to the original, he will more than adequately have performed his function.

I. Vital Statistics

The figures for general and specific mortality, outlined by Dr. Percy Stocks, show how remarkably good was the general health of the british people during those difficult years. Those rates which are usually regarded as providing an index to social conditions—infant mortality, maternal mortality, infectious diseases of childhood, etc., have all shown steady substantial reductions during the period reviewed. The birth-rate rose steadily, and the only cause of general mortality which shows significant increase is called " operations of war."

The feared epidemics did not arrive, apart from a great increase in the incidence of cerebrospinal fever in 1940, which has since slowly decreased. This was to be expected when so many young adults, and not a few children, were living in herds. Even tuberculosis, though it showed a substantial increase in 1940, has now fallen to pre-war levels.

II. General Epidemiology

This section was compiled by Medical Officers of the Ministry concerned with infectious-disease control.

Smallpox and postvaccinial encephalitis are discussed, and the bearing of experience on the policy of compulsory vaccination is clearly responsible for the stopping of compulsory vaccination by the National Health Services Act.

On diphtheria, the writers, while welcoming the steady reduction and associating it with the diphtheria-immunization campaign, point out how much more complete must be the immunized state of children before results comparable to those of North America will be achieved.

The effects of war-conditions and of new forms of treatment (especially for cerebrospinal fever) are discussed in relation to all the other infectious diseases. Some twenty cases are reported of indigenous malaria spread by *Anopheles maculipennis var. atroparvus.* It is surprising that there have not been more cases, when the number of troops returning from malarious areas is considered in conjunction with the neglect of drainage in certain saltmarsh areas occasioned by the war. In the note on tuberculosis, reference is made to the Medical Research Council's Committee on Tuberculosis in War Time, to the special problems of the military services, and to the use made in these services and in industry of mass miniature radiography. The present position and the challenge is well stated as: " pulmonary tuberculosis has hitherto been discovered at a stage later than that in which radiography has now made diagnosis possible."

The position of the civilian patient who, as a result of mass miniature radiography, was discovered to have a tuberculous affection of the lungs and who felt perfectly well and was unwilling to give up his livelihood, made necessary an insertion in social legislation providing for maintenance-allowances in certain circumstances. It is well recognized that the future value of mass radiography will depend on whether a sufficient provision of hospital and sanatorium beds can be made available for cases discovered.

The wartime increase in venereal disease is discussed especially in relation to the limited notification and compulsory-treatment powers over persons suspected of spreading widely the infection, while the section on cancer, rheumatic affections, scabies, and pediculosis, all have considered analyses of statistics and of the results of recent experience.

III. The Emergency Public Health Laboratory Service

This service, planned by the late Professor W. W. C. Topley and subsequently directed by Professor G. S. Wilson, is welcomed as a wartime scheme which has proved too valuable to be dispensed with in peace. Its value lay essentially in that the many local laboratories were enabled to keep closely in touch with Medical Officers of Health and to build up a regional bacteriological field-service. There were three central laboratories, ten (subsequently reduced to seven) constituent Emergency Public Health laboratories, and a large number of university, voluntary-hospital and local-authority laboratories, which by agreement worked in the scheme. The special investigations carried out are listed in the text.

IV. Maternity and Child Welfare

This section is divided into two parts: A. *Nutrition of mothers and infants,* and B. *Evacuation of school children and others.*

[1] [For title, particulars and price, see *Book Reviews*]

Section A is by Dr. Dorothy Taylor, and it covers the special wartime problems of evacuation of mothers and children, of the care of children evacuated without their mothers, of the provision of day-nurseries for the children of mothers in industry, and of many other arrangements which had to be made for the welfare of mothers and children.

There are some interesting tables compiled, on lines now well-known in previous reports, from detailed reports on cases of maternal deaths, but it is disconcerting to note that in only about one-half of the cases of death of a mother associated with pregnancy was a detailed report received. The statistics are invalidated completely and future statistics will also be valueless unless all cases are analyzed. It is hoped that in the National Health Service this will be remedied.

Section B by Dr. E. L. Sturdee outlines some of the social aspects of the evacuation of schoolchildren as well as refugees of all ages. Some of the experience gained has been most valuable, notably that concerning the handling in hostels of " difficult " children.

V. Food and Nutrition[2]

The story of british food-rationing, reviewed by Dr. W. A. Lethem, during the war is one of which we are proud. The irksomeness of it then (as now) receives plenty of comment, but its fairness has seldom been questioned, and this was one of the big factors in morale.

The administrative system is of personal rations for basic foods, with points varying in value for less-essential foods as the latter are available, while the pregnant woman and the nursing mother and her children are given the necessary extras. The system is founded on the three cornerstones of scientific assessment of needs, of social justice, and of rigid control. That the scientific assessment and recommendations for supplying special needs were sound, seems to be indicated by every investigation which has been made to assess nutrition.

VI A. Emergency Hospital Scheme

Sir William Jameson in his general introduction says:

> " It is hardly possible to forecast now which parts of the Emergency Hospital Scheme will prove in the years to come to have contributed most to the health services of the country."

Sir Francis Fraser and his fellow-authors show that co-operating in the scheme were every type of hospital in the country—voluntary, local-authority, teaching hospital, and the new hospitals established at the outbreak of war. It was necessary to allot medical men arbitrarily to hospitals, and to pay salaries to the honorary consultants of voluntary hospitals who had to work in the new scheme. The aims were stated as (p. 127):

> " (1) To make available approximately 300,000 beds in hospitals for civilian casualties and all Service sick and casualties for which provision could not be made by the Services. The Services' contribution was expected to be about 30,000 beds in the whole country.
>
> (2) To provide out-patient and hospital treatment in casualty clearing hospitals in vulnerable areas, and in fully equipped base hospitals outside vulnerable areas.
>
> (3) To treat in special hospitals, fully equipped and staffed by experts, certain types of injury and disease.
>
> (4) To provide adequate accommodation in hospitals for medical cases and for convalescents not requiring the resources of a fully equipped hospital.
>
> (5) To appoint Consultant Advisers to the Ministry, Regional Consultants to the Regional Hospital Officers, Regional Consultant Advisers on special subjects, Group Officers in large provincial towns and Group Advisers to other groups of hospitals in order to ensure the most efficient standard of treatment of casualties in all EMS hospitals with the view of attaining as quickly as possible the return of casualties to the highest possible degree of physical fitness."

It seems likely that these aims are easier to state now than they were in 1939!

In the early days, large numbers of beds were kept empty to receive air-raid casualties and sick military personnel. Fortunately, the former never reached the high numbers expected, so that in addition to providing accommodation for a high proportion of all military cases, the hospitals came more and more to be used for dealing with ordinary civilian patients. When civilian casualties did begin to occur, the EMS met all requirements.

Similarly the arrangements for reception of convoys of sick and wounded military cases from overseas were undertaken, so that by D-day the authorities had enormous experience of individual and group hospital administration. As a result they were never flooded, and their organization for the reception and distribution of wounded earned the well-merited thanks of the men.

The development of special centres for plastic surgery and jaw injuries, neurosurgery, orthopaedics, etc., gave valuable experience for peacetime needs, though perhaps it will be a mistake to draw too directly from such experience.

The following quotation invites some scepticism—surely we hear the same in any service in any land.

> " The chief objections to the scheme on the part of the hospitals arose from the numbers of circulars and instructions which had to be dealt with, and the number of forms and returns which had to be completed. During the inception and evolution of a service of this kind, the functions of which were constantly expanding, and in the working of which many alterations had to be made from time to time in the light of experience, the issue of many instructions and amendments thereto was unavoidable. As regards returns and forms, all were found to be necessary for the purposes of records and statistics, but their completion undoubtedly threw a heavy strain on the depleted staffs of the hospitals. This state of affairs, attributable to war conditions, would not obtain to the same extent in normal times, and would have been less burdensome if a more generous establishment of clerical staff could have been authorised." (P. 157.)

That " all [returns and forms] were found to be necessary for purposes of records " makes it clear that those who called for returns were gifted to a degree uncommon in mortals!

Another statement which leaves an uneasy feeling is:

> " The inconvenience caused to patients by their treatment being carried out in hospitals at some distance from their homes is unavoidable, but is of minor importance in view of the benefits patients receive under this system.
>
> The Emergency Hospital Scheme therefore provides an example of a system under which the interests of the State, the hospital authorities, the medical profession and above all the patients were as fully provided for as the somewhat restricted resources in the circumstances imposed by war conditions would permit. It would appear to have been appreciated by all concerned." (P. 157.)

[2] [See *BMB* 1029 in this number for a review of wartime food-rationing.—Ed.]

VI B. The Hospital Pathological Service

This service was set up by Dr. P. (now Sir Philip) N. Panton and is described by him in the report.

Before the war, in conjunction with the British Medical Association and the Ministry of Labour, a national register was formed of all people (about 2,500) working in hospital laboratories.

In "designated" laboratories, the whole cost of the service was borne by the Ministry. The "non-designated" laboratories were those which received payment for work done, the sector pathologist having a purely advisory and consultative interest.

The early survey, and those carried out after war started, showed that in the smaller country hospitals, laboratory and staff provision was quite inadequate. The system adopted was to make as many regions as there were medical schools, to appoint the professor of pathology as honorary adviser for each area, and thereafter to make the best possible arrangements with the manpower available in the areas.

The civilian blood transfusion service. A regional blood-transfusion service was set up under the Emergency Medical Service (EMS), and blood-banks were established in provincial cities, associated when possible with a university.

This service, which is now a well-established regional organization of the Ministry of Health, has been an immensely valuable gain. Its present availability, to say nothing of future expansion, is of immense service, and is likely to prove essential to the study of the distribution of the Rh and other blood-group factors.

VII. Civil Defence Casualty Service

This section, while of great historical interest and of future value, in that it gives an account of sociological experience in the needs of old people, will not be reviewed as most people are familiar with the story of the air-raid casualty, and the problems of the air-raid shelter and of the homeless.

VIII. Problems of Medical Man-power

The problem of the correct allocation of manpower for civil and military needs arose early in the war, and in December 1940, a government committee was appointed to consider the matter. As a result a central and regional medical manpower committee organization was established and, by compromise, a reasonably fair distribution was always achieved.

IX. Dental Services

The National Health Insurance and Maternity and Child Welfare Dental Schemes carried on under severe handicap during the war. Fruitful collaboration of dentists and surgeons in the special centres for maxillofacial injuries resulted in special courses, notably at the Queen Victoria Cottage Hospital, East Grinstead, where the training given to specialists enabled them to carry out excellent teamwork both in the armed forces and in EMS hospitals.

X. The Nursing Services

The shortage of trained nurses and recruits to the profession is likely to be one of the major difficulties encountered in the provision of a National Health Service.

A Nursing and Midwives Division was created in the Ministry of Health in 1941 to deal with general and professional questions. A Chief Nursing Officer and two Deputies at the Ministry are represented by 21 women inspectors, 12 regional nursing officers, and 11 deputy regional nursing officers.

The inspectors' work in supplying nursing needs and services in wartime is to be continued, and they also have as duties the inspection of maternity and child-welfare schemes of local authorities. The duties of the inspectors are not given in sufficient detail for a Medical Officer of Health (or indeed any reader) to judge the probable value of inspectors in the future. There is an excellent account in this section of the present difficulties and the attempts to meet them.

XI. Morbidity Statistics

The well-known lack of statistics concerning morbidity as opposed to mortality has troubled all british medical statisticians and planners from John Graunt and William Farr onwards. Dr. Percy Stock's analysis of a sample of 45,000 cases (⅛ of total) admitted to EMS hospitals in 1942 and 1943 has therefore been eagerly awaited, as will be the promised more-complete estimates when time permits analysis of the other records.

The age- and sex-incidence of acute and chronic, severe and mild diseases, and the duration of disability, are analyzed in a series of tables. The following extracts are from those chosen by Dr. Stocks himself:

"... *Neoplasms* accounted for 17 per 1,000 non-infective and non-respiratory diseases amongst men and 32 amongst women, the rates increasing rapidly with advancing age. *Diabetes* rates were only 1 or 2 for men under 45, increasing to 36 at ages 55 and over. *Anaemias* showed a rate of 9 per 1,000 women compared with 1 for men. For *Psycho-neuroses* and functional digestive disorders together the rates amongst men of the 5 ages were 81, 107, 109, 94, 18 in 1942 and 79, 98, 115, 88, 19 in 1943, reaching a maximum at 35–44 and then falling; amongst women the rate was about 80 at each age under 35. *Eye* and *ear* conditions gave rates about 11 and 27 respectively for men; compared with 8 and 21 for women. Diseases of the *heart* and *arteries*, together with cerebral haemorrhage, showed rates increasing rapidly with age after 35. For diseases of the *veins* men's rates were much higher than those of women, averaging about 80 at all ages and reaching a maximum at 35–44. *Acute sore throat* showed a remarkable decline with advancing age for both sexes, rates being about 100 at ages under 25, falling to about 40 at 35–44 and 20 or less after 45. This was true also of acute *hepatitis and jaundice* amongst men; and 1943 rates were considerably higher than in 1942 for both sexes. *Hernia* rates amongst men varied little with age up to 55, being about 60, compared with 4 for women.

Gastric and duodenal ulcer rates for men were as follows:

		15 –	25 –	35 –	45 up	All ages	Scottish
Duodenal	1942	17	31	44	52	29	52
	1943	12	28	44	32	26	45
Gastric, etc.	1942	3	8	16	8	8	9
	1943	3	7	13	23	7	3

Out of 1,623 at ages under 45 there were 1,278 with duodenal ulcer, giving a ratio of 1 gastric to 3.7 duodenal, pyloric ulcer being included with the former of which they formed 8 per cent. The total ulcer rate for women under 25 was only one-sixth of that for men of the same age group, and at 25–34 one-tenth." (p. 217).

To appreciate their value fully, the tables must be studied in detail.

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USAGE OF DDT

Dr. J. R. BUSVINE

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The story of the discovery and development of DDT as an insecticide gives an interesting impression, not only of the ramifications of applied science, but also of the complexities of modern needs. Nowadays all kinds of people require insecticides for coping with a great variety of pests whose attacks and depredations were formerly regarded as inevitable. DDT has received a great deal of publicity and has become very widely known. But there has been a danger that too much adulation will lead to disillusionment, for DDT has its limitations and it must be properly used. It does not act, for example, as a fumigant or repellent; it must come into direct contact with an insect to kill it. Therefore puffing DDT solution or powder into a wardrobe cannot be relied on to protect clothing from moths unless each garment is properly impregnated. Again, the rather slow action of DDT may give rise to disappointment.

If it is useful for the general public to understand the proper doses and ways of using DDT, such information is essential to scientific, medical and sanitary officials who deal with insect-pests. But so rapid has been the enlargement of the field of knowledge about DDT that these men have found it difficult to keep abreast. The comprehensive summary[1] of Campbell & West of published work on DDT up to 1945, is therefore very welcome.

After a historical chapter, the first section of this book deals with DDT rather from physical and chemical aspects. The methods of manufacture, reactions of DDT and analogous compounds and, especially, methods of preparing it for use, are considered in detail. On the whole, this section is excellent, though perhaps some caution is necessary in interpreting the results observed with formulations which are still undergoing trial. For example, the incorporation of DDT into paints and certain other materials does not yet seem to have been clearly justified. The next section of the book reviews the results obtained against a variety of insect-pests, the original papers being summarized very briefly but usefully, with emphasis on quantitative data. These pests are grouped into chapters in accordance with their relations to man, which is convenient; but it is less easy to justify their arrangements within the chapters in the arbitrary alphabetical order of common english names.

A summary of information about DDT of a somewhat different type is available in a pamphlet produced by the Ministry of Supply.[2] Within quite a small compass there are many data useful for compounding and using the insecticide (e.g. lists of solubility in different liquids). The experimental results against various insect-pests are given briefly; the list of pests against which DDT has been used is imposing but not really helpful. However, there are general directions for dealing with different types of pests and quantitative data for common ones. In the appendix there are given some "typical formulations," but perhaps too much emphasis is laid on aerosols which do not utilize the persistent residual powers of DDT.

As summaries of research on DDT, these two publications cannot remain up-to-date for very long, but this fact does not greatly detract from their value. Both of them give many chemical and physical data which are required for preparing and using DDT. They give formulae for practical applications which have in most cases been established as workable even if they are not the best possible. The book by Campbell & West gives in addition a comprehensive account of all the early work on the subject which ought to be consulted before embarking on further research.

[1] [For title, particulars and price, see *Book Reviews*]

[2] [For title, particulars and price, see *Book Reviews*]

PUBLIC HEALTH IN BRITAIN 1939–1945

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The second source of morbidity statistics which is available as a result of the war is the figures of incidence of sickness in a random selection each month of about 7,000 persons between 16 and 64 years of age. The War-time Social Survey placed its organization and field-workers at the disposal of the Ministry for the experiment which began in the winter of 1943–44. Subsequently older people were included. The survey is continuing, and the next step will be to include children.

In this case also, to abstract is impossible—the information is already compressed in the report.

XII. Advances in Therapeutics

There is nothing new in this useful survey by Dr. W. P. Kennedy, of the advances in chemotherapeutic agents, antibiotic substances and the new insecticides, but it is well worth reading because of the information given about the steps taken to meet such pressing problems as the loss of javanese quinine, the commercial production of penicillin, etc.

XIII. International Health and Medical Intelligence

Dr. Melville Mackenzie in this section shows how some of the difficulties were met of collecting information about epidemic conditions in enemy-occupied countries, and how the Ministry of Health fulfils its obligations under the International Sanitary Convention 1926.

XIV. Environmental Hygiene

This is short, and deals with the work of the Ministry connected with wartime building, air-raid shelters and the Water Act 1945, which is framed to provide in all rural areas a piped water-supply.

XV. Health Publicity

It is delightful to discover that the national newspapers refused to allow advertisements which said "Always wash your hands after using the W.C."

XVI. Planning for the Future

This section was written by Dr. J. A. Charles before the publication of the Bill which became the National Health Services Act in November, 1946, so that it is alined on the White Paper issued by the Coalition Government in February, 1944. Nevertheless, it is an excellent summary of the situation which made a National Health Service inevitable, and as such should be read by all who would understand the full implications of the new Act.

The surveys and preliminary planning which began in the dark days of 1941 illuminate the faith in a bright future which was also so conspicuous a feature of the Beveridge Report. Without the results of regional hospital-surveys carried out in 1941–45, the establishment of the hospitals service would have been delayed by just so long as it would take to carry out, digest and discuss new surveys.

Annotations & News

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SOCIAL MEDICINE AT OXFORD

The Institute of Social Medicine, Oxford, came into being with Professor John A. Ryle as director in April, 1943, but it has published only one annual report[1] as, because of staffing and accommodation difficulties, 1945 represents the first year of work.

The purposes of the Institute, as laid down in the Resolution of the Trustees, are as follows : (*a*) To investigate the influence of social, genetic, environmental, and domestic factors on the incidence of human disease and disability; (*b*) to see and promote measures, other than those usually employed in the practice of remedial medicine, for the protection of the individual and of the community against such forces as interfere with the full development and maintenance of man's mental and physical capacity; (*c*) if required by the University to do so, to make provision in the Institute for the instruction in social medicine of students and practitioners of medicine approved by the Board of the Faculty of Medicine in the University of Oxford.

The section of vital statistics, clinical department and radiographic department constitute the main departments at present and, separately or in combination, the staff has launched an ambitious programme. A large number of infants is enrolled for the purpose of follow-up and study on first attendance at the city's Child Welfare Centres. It is intended to examine these children clinically at three-monthly intervals and to record by *x* ray skeletal development by means of standardized photographs at six-monthly intervals. In the first instance it is hoped to observe all these children for five years.

In co-operation with Morris Motors, Limited, an extensive study of occupational morbidity has been started.

After a first enquiry had given the necessary experience to establish a standard method of examination and records, an investigation has started on children aged 11–15 in several districts. It is intended to determine the relationship of thyroid enlargement to the iodine-content of the drinking-water.

The main work of the radiographic department is connected with the establishment of standards of normality of *x*-ray appearances of skeletal structure.

Forty-two pairs of twins are being observed, and their resemblances recorded. This is intended to be a pilot for wider studies.

A large-scale statistical enquiry on stillbirths and neonatal mortality is being made in relation to environmental and social factors. These, with other smaller investigations, give some idea of the vast scope of the programmes contemplated. The results will be anticipated most eagerly.

A. C. Stevenson

1033

SOME LITERARY BY-PRODUCTS OF THE CHEMICAL INDUSTRY

There are some literary by-products of the chemical—and, more particularly, the pharmaceutical—industry which are so familiar that they need no description here. These are the circulars, pamphlets and booklets in which proprietary products are advertised to their potential users, sometimes by the provision of essential technical information that is not conveniently available elsewhere.

In a rather different category are the several periodicals published by pharmaceutical manufacturers. These are usually not devoted exclusively to advocacy of the manufacturer's products, but their purpose is nevertheless the direct stimulation of interest in the goods manufactured.

Of recent years there have been some examples of the publication by the chemical industry of periodicals or other literature having no direct relation to the firm's products, except that they may include advertisements. Why does the chemical industry make itself responsible for such publications? Presumably they were started because it was thought that they would contribute to the general prestige of the firms responsible. It is probably impossible to prove whether they have this effect or not—or whether such an effect would be reflected in increased sales of the firm's products. But quite apart from the question of a utilitarian motive, there is no reason for supposing that industrialists are less susceptible than other publishers to the direct satisfaction that comes from publishing something that is good and valuable in itself.

There are now at least two periodicals—one british and the other swiss—published by the chemical industry which are of high cultural value. The first of these is *Endeavour*, which is published quarterly by Imperial Chemical Industries, Ltd., and has now reached its sixth volume. It publishes articles by distinguished writers on a wide variety of scientific subjects, including the history and philosophy of science. A special feature of *Endeavour* is the attention given to its physical production. The typography and lay-out are arresting, without being meretricious, and the illustrations—especially those in colour—are often remarkably fine. In short, the high standard of the matter is fully matched by the technical standard of production, as befits a journal which treats science as an aspect of culture.

The second of these periodicals is the *Ciba Zeitschrift*, to which we have previously referred.[1]

This is a monthly (published less frequently since the war) journal devoted to the history of medical science, the medical profession, and related subjects. The first number appeared in September 1933, and in March 1946 the 100th number was published. This number contains more than the usual number of pages, and its subject—*Die Injektion*—is one of more than usual interest. Its author, Dr. H. Buess, devotes most of his space to a detailed and absorbing study—probably the best available account of this subject—of the history of intravenous injection, but he also discusses more briefly the origin of the use of the subcutaneous and intramuscular routes. Subsequent numbers have been on *Die Ueberwindung der galenischen Anatomie* (No. 101, May 1946), *Die Initiation* (No. 102, July 1946), *Gehör und Hören* (No. 103, October 1946) and *Die medizinische Fakultät von Paris* (No. 104, January 1947).

In 1942, a special number of the *Ciba Zeitschrift* was published in celebration of the 60th birthday of the president of the Ciba company—Dr. J. Brodbeck-Sandreuter (since deceased). This volume of 184 pages is devoted to various aspects—ethnological and historical; scientific and technical; legal—of drugs and their preparation, and all of the 31 articles are written by members of the company's staff. In the same year, a Festschrift to Dr. Brodbeck was also published. This clothbound volume of 449 pages was edited by Dr. Karl Reucker, editor of the *Ciba Zeitschrift*, and it is a satisfying example of the fine printing of Benno Schwabe of Basel. The introductory article by the Dean of the Medical Faculty at Basel, Dr. A. Werthemann, is followed by 10 interesting papers, of which we would select for special mention Dr. A. Schmid's contribution on the history of electrotherapy (pp. 73–121), a paper by Dr. H. Buess on the development of the doctrine of irritability (pp. 229–333) and Dr. Fritz Husner's catalogue (pp. 137–269) of the Basel medical theses from 1575–1829. The last includes author- and subject-indices and is a work of permanent bibliographical value. Other contributions are on medico-historical research in Switzerland (H. Karcher), the development of observations on electrical manifestations in animals and man (O. Merkelbach), and the early printing of medical works in Basel (A. Pfister). The numerous plates illustrating Dr. Pfister's article include some beautiful reproductions of the hand-coloured copy of the *Fabrica* in the library of Basel University.

Another Festschrift emanating from the chemical industry, but one of a different kind, is the Jubilee volume dedicated to Dr. E. C. Barell, president of the Hoffman-La-Roche company in Basel, on the completion of 50 years' association with the

[1] [For title, particulars and price, see *Book Reviews*.]

[1] [See *BMB* 794/17–-Ed.]

company. This clothbound volume of 468 pages contains 34 papers written by members of the scientific staff of the Roche organizations in Basel, England, and the USA. About half the papers describe original work on vitamins, the other subjects including contributions on synthetic analgesics, drugs acting on the autonomic nervous system, and antibiotics. The volume is an impressive testimony to the scientific resources of the Roche organization, as was doubtless one of its intentions.

A peculiarly attractive smaller volume published by the Ciba company—*Schweizer Aerzte als Forscher Entdecker und Erfinder* [swiss doctors as researchers, discovers and inventors]—was produced for an exhibition of books and manuscript illustrative of this theme. This is much more than a catalogue : it is a collection of miniature bio-bibliographies (accompanied in each case by a portrait) of 60 swiss doctors, starting with Vadian (1484-1551) and ending with Rorschach (1884-1922). Each subject occupies exactly two pages, and to secure this uniformity of plan must have demanded considerable ingenuity and much detailed work. On perusing this volume, one is struck by the great number of famous names in medicine that Switzerland has produced. Paracelsus, Conrad Gesner, Felix Platter, the Bauhins, Peyer, Brunner, Haller, Coindet, Koelliker, Goll, His, Forel, Kocher, Sahli, Bleuler, Yersin—these names are all a part of medical history.

The last volume to be mentioned here is the most remote from any apparent connexion with industry. It is a paper-covered anthology of french verses referring to the medical profession, published by Ciba in 1945 under the title *Vers et médecine*. The text is accompanied by numerous reproductions of the Daumier caricatures which first appeared in Fabre's *La Némésis médicale*. Many of the verses are satirical, and they range in period from the Middle Ages to the 19th century. The collection is an enchanting one, and a valuable antidote to professional self-satisfaction. Here is a description of " Le médecin des dames " —a type which is by no means extinct today. In fact, the third and fourth lines might be interpreted as referring to certain forms of psychotherapy in a sense far more literal than their author could have imagined :—

Sur papier rose ou de Chine
Il met ses ordres du jour,
Et parle de médecine,
Comme l'on parle d'amour.
Plus fin que ses camarades,
Jamais il ne risque rien ;
Car il ne prend de malades
Qu'autant qu'ils se portent bien.

The same writer, Eugène Scribe, satirizes the contemporary craze for treatment by acupuncture :—

Pour guérir, on vous pique;
Système economique,
Qui, depuis ce moment,
Répand
La joie en nos familles;
Car nous avons en magasins,
Plus de bonnes aiguilles
Que de bons médecins.

Now, we think it absurd that patients should be treated by perforation with needles. Nevertheless, the same treatment, camouflaged and sanctified by pseudo-science still exists : but today the needles are hollow, and through them are squirted vaccines or glandular extracts of no demonstrable activity. Again, what are we to say of the 20th-century therapist who will, on some wishful and doctrinaire assumption, solemnly withdraw blood from the patient's vein and inject it into his buttocks ?

The chemical industry has brought great gifts to therapeutics, but it is equally true that it has not been slow to capitalize the follies of medicine. The literary by-products which are the subject of these notes are, in their various ways, among the industry's more welcome contributions.

N.H.-J.

1034

HEALTH OF LONDON

London County Council is by far the largest local authority in Britain so that the Report[1] of the County Medical Officer of Health and the School Medical Officer is always of much more than local interest. [Overseas readers should remember that London County Council boundaries are not those of greater London—the mid-year population, 1945, of the County Area was 2,601,370.]

Mortality and morbidity figures departed from their prewar trends, though the incidence of most diseases related to social conditions is again back almost to prewar level. Intestinal infections have, however, increased in recent years. Two cases of smallpox and a case of typhus fever occurred, all contracted overseas, and there were no secondary cases.

Measles (23,518 notifications) was more prevalent than for many years and was by far the commonest infectious disease. The death-rate from measles was 0.012 per 1,000 of the population.

Maternal mortality was 1.93 per 1,000 live births compared with 1.84 for the rest of England and Wales, while the infant mortality-rate of 44 per 1,000 live births is the lowest ever recorded in London.

The large hospital service has been severely taxed by war conditions. Staff has been directed elsewhere, hospitals have been taken over, and so on; nevertheless, in addition to the usual work many thousands of military cases from the various battlefields were accommodated.

The outline of the scope of research work being carried on is of great interest in view of the fear of many medical men that they would be " regimented " in a big service.

In the section of the report on the school health service the most important change is, of course, the coming of the Education Act, 1944. Arrangements have already been made whereby all schoolchildren can have comprehensive free treatment in the Council hospitals or at voluntary hospitals.

The number of routine medical inspections of pupils is still less than half those made each year before the war, but the special provisions for handicapped pupils in which London has been so active have increased in spite of all difficulties.

This Annual Report is still much smaller than before the war, largely because comment on statistics and on the activities of the Health Department has been reduced.

A. C. Stevenson

[1] [For title and particulars, see *Book Reviews*.]

1035

AN IMPORTANT NEW ABSTRACTING SERVICE

There has long been a need for an abstracting journal to cover general medicine. This need is rendered more acute by the prodigious growth of medical periodical literature, which has, since the conclusion of the war, once again taken an upward curve.

Two new periodicals published by the British Medical Association—*Abstracts of World Medicine* and *Abstracts of World Surgery Obstetrics and Gynaecology*—made their first appearance at the beginning of the present year and, judging from the early numbers, they will effectively perform the important task of providing an abstracting service in general medicine and surgery. Both journals are selective—they do not attempt to include every relevant paper published—and, considering the subject-range covered, readers may feel grateful that there has been no concession to the neurosis of comprehensiveness. So many " original " papers published in the world's medical press are the product of little but the desire to publish, that " comprehensiveness " would often imply the artificial prolongation of the life of that which were better never born. The adoption of a selective policy implies that, for every abstract published, many articles in different languages will have been scrutinized and rejected. There is therefore far more work involved in an abstracting service of this kind than is immediately evident to the reader.

We understand that over 1,000 periodicals are already passing regularly through the editorial offices of these journals, and they will ultimately amount to twice or three times the present number. These figures give some measure of the task that has been undertaken. They also indicate the value to the reader of such a service. Few men can hope to digest the contents of more than a very few journals in their original form, and few have the linguistic knowledge to read all journals of potential interest.

Perhaps it is the medical, surgical, and obstetrical specialists who will find these abstracting journals the most useful. But they will also be of great value to the worker in laboratory medicine who wishes to preserve contact with the broad and ever-widening stream of medical progress. In this connexion, it may be added that there is in the selection of material a commendable emphasis on experimental medicine. The general practitioner who has the time to read, and who attempts the increasingly

difficult task of maintaining some awareness of what is happening in medical science, would find a subscription to *Abstracts of World Medicine* an excellent investment.

The abstracts are " informative ", as opposed to " indicative ". That is, each abstract is a precis of the original article, and contains the important quantitative data of the original. The publishers state that " No abstract can be regarded as a substitute for the article abstracted ", but this is surely a rather unrealistic assertion. Libraries, university departments, and the few private individuals who subscribe to the special journals will still require the originals, and the effect, if any, of an abstracting journal on the circulation of the original periodicals is probably favourable. On the other hand, there is a vast number of readers of more general interests for whom the only feasible alternatives are to learn of the work reported in the original either at second-hand or not at all.

A few words may now be said on the background of this new abstracting service. It is fitting that the first appearance of the two new journals should coincide with the succession of Dr. Hugh Clegg to the editorship of the *British Medical Journal*, for it was Dr. Clegg who, while deputy-editor, saw the need for such a service and took the entire responsibility for its planning and execution. The service is conducted under the general direction of Dr. Clegg, with Dr. G. M. Findlay as editor. Dr. Findlay has had a distinguished career in medical research, and is the author of *Recent advances in chemotherapy*, of which a new edition is in preparation. This book was one of the best of the excellent *Recent advances* series. The assistant editor is Dr. S. S. B. Gilder, who numbers among his accomplishments an exceptional knowledge of modern languages, which was largely gained during years spent as a prisoner-of-war. The editorial staff also includes a well-known expert in medical bibliography—Mr. L. T. Morton—and several exponents of other special talents and qualifications.

Finally, a tribute must be paid to the British Medical Association for having had the enterprise and vision to sponsor this substantial and important contribution to medical literature.

N. H.-J.

1036

MEDICINE AT THE CROSS-ROADS

There must be few, if any, branches of natural science that are so burdened with tradition as medicine. Our classification and nomenclature of disease, the divisions of medical practice, and the medical curriculum to which the student must submit, bear all too plainly the evidences of their origins in the obsolete past.

The student is burdened with the necessity of spending valuable time in the minute study of topographical anatomy for no better reason than that anatomy was, less than a century ago, almost the sole medical subject about which any positive knowledge was available. Medical specialization arose at a time when medical theory was still dominated by a solidist pathology, and the clinical specialities consequently have a predominantly topographical basis—the patient being arbitrarily divided into organs or regions, each of which is claimed as the province of a different kind of specialist. Although a high pitch of technical perfection has been reached in many of these clinical specialities, there is a growing awareness that most of the advances in medical knowledge are the product of studies which have little or no relation to the arbitrary divisions of medical practice.

Professor Neergaard is one of those who have asked themselves whither medicine is going, and whether it can even claim an existence as an independent discipline. In an essay[1] of 317 pages, he has much to say on some fundamental and fascinating problems of medicine. A superficial study of this essay does not reveal a closely-reasoned argument, and there is a great deal of repetition. The author would have done his readers a great service if he had included somewhere a concise statement of his argument and conclusions. He makes much of the alleged loss of faith in scientific medicine, and the rising influence of nature-cure medicine (Naturheilmedizin), but whatever may be the position in Switzerland, such cults could hardly be regarded as serious competitors to orthodox medicine in the english-speaking world.

Neergaard also points out that medical science is based on the classical physical conceptions which are now discredited by modern physicists. While the " mechanistic " conceptions of modern medicine have led to great successes, the phenomenon of disease, he says, has its own peculiar laws and, in pursuit of these, medicine will evolve from an applied science to an independent scientific status—an autonomous medicine (autonome Heilkunde). This contention seems to involve a highly subjective attitude to " disease ", by which it is promoted to the status of an independent " entity ". " Disease " is a term applied to certain biological phenomena which human beings find inconvenient, and it is difficult to see why such phenomena, which involve a multiplicity of different biological situations and mechanisms, should be unified by obedience to distinctive biological " laws ".

What exactly is meant by a " dynamic reaction-pathology " is not at all clear to the reviewer, although the author devotes 11 pages to explaining it. The term seems to be used throughout the book as a sort of slogan.

The chief interest of Neergaard's essay is in the train of speculations aroused in the reader by some of the questions posed. The conclusions are diffuse and difficult to grasp. What can be grasped seems to reflect more the personal convictions of the author than a well-grounded philosophy of medicine.

N. H.-J.

[1] [For title and particulars see *Book Reviews*.]

1037

QUE SAIS-JE ?

The present state of knowledge

In the course of recent months, we have received eight examples of an interesting series of books published by the *Presses Universitaires de France* under the collective title *Que sais-je*? The series is edited by Paul Angoulvent, and comprises a list of titles ranging over a remarkable variety of subjects: scientific, technical, historical, literary and artistic. These little books, which may perhaps be compared to the *Pelican* series in English, are designed to present brief readable surveys of the subjects concerned for the benefit of all intelligent readers, specialist or non-specialist. They are written by experts in a scholarly manner, without being encumbered with the wealth of detail contained in a textbook. Most of those we have seen include a historical survey and end with a summary of the present state of knowledge, future possibilities and general significance of the subject.

The format is handy, the type clear, and the general standard of production good. Those subjects that lend themselves to illustration are well supplied with diagrams, tables, graphs, sketches, etc. In the examples we have seen, no complete bibliographies are supplied, but in many cases there are short lists of books, or references are given in the form of footnotes.

The eight books with which we are concerned here fall roughly into three categories; five of them are to a greater or less degree physiological, one is on climatology, and the other two are concerned with evolution, genetics and heredity. No. 8 (*Le système nerveux et ses inconnues*, by Paul Chauchard, 1944) deals with the mechanism of nervous function. This is in some sense a companion volume to no. 181, by the same author (*Le moteur vivant*, 1945) which gives an account of the action of the muscles and their control by the nervous system. No. 188 (*La psychophysiologie humaine*, by Jean Delay, 1945) is again closely connected by its subject-matter with no. 8. No. 5 (*Comment se défend l'organisme*, by Léon Binet, 1943) describes the defence-mechanisms of the human body and how they react when confronted by cold, heat, pain, fear, asphyxia, haemorrhage, shock and burns, hunger and thirst, attacks on the respiratory system, and by food-poisoning. No. 194 (*Le sang*, by Louis van den Berghe, 1946) is an account of the blood: functions, composition, pathological variations, blood-groups and blood-transfusion. No. 171 (*Les climats et l'organisme humain*, by Emile Duhot, 1945) gives a description of the effects, both good and bad, that climate has on the human body. The two remaining volumes, no. 113 (*Génétique et hérédité*, by Maurice Caullery, 1943) and no. 141 (*L'origine des espèces*, by Emile Guyénot, 1944) supplement each other to some extent. The authors summarize the present position in their respective fields.

This series is to be warmly commended to the medical or scientific reader who wishes at the same time to improve his French and his knowledge.

A. H.-S.

1038

SWISS ACADEMY OF MEDICAL SCIENCES

The Swiss Academy of Medical Sciences was founded at Basel on the 24 September 1943, to advance medical and biological science both in Switzerland and elsewhere. Its function is to act as a national council of research linking the medical centres of the country, all university faculties of medicine and the swiss medical profession. Its aims, based on the principle of free scientific research, are: to subsidize swiss scientific research both at home and abroad; to improve the knowledge of swiss scientists, to encourage by means of scientific gatherings, special commissions and other methods, the collaboration of swiss men of science; to establish relations with foreign scientists, especially swiss doctors working abroad; and to publish scientific works or finance their publication. The first number of the official organ of the Academy, *Bulletin der Schweizerischen Akademie der Medizinischen Wissenschaften*, appeared in February 1944, published by Benno Schwabe & Co., Basel, and we have now received the first volume. Volume I, no.1 contains an account of the foundation of the Academy, its statutes and of the *Bibliographica Medica Helvetica* (for review of this see *BMB*, 1946, **889**). In volume I, no. 3, will be found the first Annual Report of the Academy for the year 1943–44, a highly satisfactory record of work projected and accomplished. Original articles appear in each number in german or french, each accompanied by summaries in german, french, italian and english. Like all the medical publications of Schwabe that we have seen, the technical standard of printing, paper and production is high.

H. A. I.

1039

A NEW ANAESTHESIA JOURNAL

The year 1946 witnessed not only the celebration of the centenary of the first operation under general anaesthesia in Britain, but appropriately the first issue of a new periodical devoted entirely to the study of anaesthesia. ". . . it has become obvious for some time," writes the editor, Dr. C. Langton Hewer, in the first number, October 1946, " that the rapid advance in all types of anaesthetic and analgesic technique requires fuller and quicker expression than can be provided in the over-loaded columns of the general medical press . . . The full and accurate presentation of observations, theories, new methods, etc., is essential if a true advance is to be maintained and if unprofitable detours are to be avoided. Original contributions dealing with any aspects of the subject will be welcomed, the sole criterion for acceptance being their merit in the opinion of the Editorial Board, subject to space being available for reasonably quick publication. It is hoped that our colleagues abroad will also give us the benefit of their observations and views."

Anaesthesia: Journal of the Association of the Anaesthetists of Great Britain and Ireland will therefore be primarily a scientific periodical, but it will act also as the official organ of the Association. As it is to appear quarterly, it will be able to publish details of the Association's activities as well as news of general interest without undue delay. Book-reviews and abstracts from the current literature are also included. Volume I, no. 1, contains the history and activities of the Association summarized by its first President, Dr. H. W. Featherstone; an account of the early history of anaesthesia by the present President, Dr. A. D. Marston; and in addition to other original articles there is a reprint of the paper by Dr. John Beard on the anaesthetist and care of the surgical case, which originally appeared in the *British Medical Bulletin* celebrating the centenary of anaesthesia (*BMB* **826**). Volume II, no. 1, January 1947, contains an account by Dr. Eunice M. Christensen of the history of cocaine from the earliest times up to the isolation of the pure alkaloid; and a discussion of cauda equina lesions following spinal analgesia by Dr. Tom Dinsdale.

Anaesthesia is attractively produced and is published for the Association by George Pulman & Sons Ltd., 24 Thayer Street, London, W.1. The price is 10s. per number. We are sure that this new periodical, which will assemble british contributions to the science and practice of anaesthesia, will be warmly welcomed by anaesthetists of all countries.

H. A. I.

1040

GENERAL MICROBIOLOGY

Another new specialist periodical which will fill a gap in british biological literature is the *Journal of general microbiology*, the first devoted exclusively to the study of microbiology to appear in Britain.

This new journal is conducted by the Society for General Microbiology, formed just over two years ago as a result of preliminary work done by a committee representing the various aspects of microbiology which met in 1943 under the chairmanship of the late Sir John Ledingham. This committee felt that the lack of contact between the various branches of microbiology impeded the development of the science as a whole, and decided to form a society which would provide a common meeting-ground for those working in the various specialist fields. At the inaugural meeting on 16 February 1945, at the London School of Hygiene and Tropical Medicine, it was decided that the Society should concern itself with the study of bacteria, viruses, microfungi, protozoa and microscopic algae in their various biological activities, and more particularly, the fundamental aspect of the study of these forms including their structure and development, physiology, nutrition, chemotherapy, systematics and ecology. The journal is edited by B. C. J. G. Knight and A. A. Miles; the associate editors are G. C. Ainsworth, W. B. Brierley, T. Gibson, A. T. R. Mattick, K. M. Smith, A. W. Stableforth, and D. D. Woods, and it will publish original research in the field covered by the Society's activities.

The *Journal of general microbiology* is published by the Cambridge University Press, Bentley House, 200 Euston Road, London, N.W.1, and for the time being there will be three numbers a year, the annual subscription being 50s. The contents of volume I, no. 1, January 1947, will be found listed in the *Guide to Journals* (*BMB* **1098**) in this issue.

H. A. I.

1041

RECENTI PROGRESSI IN MEDICINA

Recenti progressi in medicina is a new periodical, published in Rome by " Il Pensiero Scientifico ", of which we have now received the first six numbers. As its title indicates, it consists of reviews, mostly borrowed from british and american sources, of recent progress in a particular field of medical science.

The editorial board is conscious of the need, especially among the younger elements in the italian medical profession, for keeping abreast with the advances in medical knowledge achieved during the years that Italy was cut off from the rest of the world. As Professor Bastianelli writes in his preface to volume I, no. 1, Ottobre 1946, " We wish to help all doctors who want to understand and to use the knowledge of today and tomorrow."—a task in which he is confident the periodical will have the assistance of the best elements in the medical profession throughout Italy. A warm tribute is paid to the collaboration of the British Council and of the medical section of American Relief for Italy, both of which provided not only assistance and advice but much selected material for translation. Recent numbers have dealt with the pneumonias, chemotherapy, meningitis and malaria. In addition to the review-articles surveying recent developments, sections are devoted to abstracts, laboratory methods, lists of the contents of important foreign medical periodicals, book-reviews and book-lists. We welcome this well-produced publication, and feel sure that it will go a long way towards bridging the gap in italian medical literature resulting from the war years.

H. A. I.

1042

SOUTH AMERICAN MEDICAL PERIODICALS

One of the best-known and oldest-established of argentine medical periodicals is *La Semana Médica*, Buenos Aires. The number celebrating its jubilee, 1894–1944, has now reached us. It contains 796 pages and is divided into sections dealing with infectious diseases, social medicine, microbiology and parasitology, neurology and psychiatry, odontology, pediatrics, radiobiology and physiotherapy, therapeutics and pharmacology, and a miscellaneous section.

Of special interest are a historical survey by Dr. Gregorio Aráoz Alfaro of the growth of hygiene and public health services in Argentina from the time when she gained her independence from Spain, a study by Dr. Francisco de Veyga of the complex problem of the declining birth-rate among the white races, and an article on the historical aspect of paediatrics in Buenos Aires by Dr. Juan P. Garrahan. This article is followed by a biographical appreciation of the work done in pediatrics, both as practitioner and teacher, by Dr. Angel M. Centeno, who died in 1925, contributed by Professor Mamerto Acuña, himself an eminent contemporary pediatrician working in Argentina. The miscellaneous section contains an article in Portuguese by Professor A. Austregesilo on the advantages in mental training to be derived from a scientific education.

* * *

We have received two other periodicals from Buenos Aires, the first of which, *Revista Oral de Ciencias Médicas*, is now in its 11th year of publication, but with this issue, no. 118, July 1946, it is to be considerably enlarged in order that it may the better disseminate knowledge of recent advances in medicine. This number contains eight original articles, and the text of the address of welcome to Sir Howard Florey on the occasion of his installation as an honorary member of the Academia Nacional de Medicina. In addition, there is a section devoted to book-reviews and abstracts, and a further section gives reports of medical meetings and congresses.

* * *

Archivos de la Secretaria de Salud Pública de la Nación, Buenos Aires is, however, a new publication of which volume I, no. 1 appeared in December 1946. Its object is defined as the formation of an intellectual link between the medical profession and the medical auxiliary services. It is intended that the journal should concern itself especially with matters relating to social medicine, including public health, social services, hygiene, etc.

The first number of the journal contains the text of the address given by Dr. Ramón Carrillo on the occasion of his assuming the office of Secretary of Public Health in Argentina, and also the text of his discourses on the subject of decrees made in the interests of public health and on various aspects of social medicine. There are further articles on the forms of assistance available to the chronically unfit, and on anti-yellow-fever inoculation in Paraguay, and the journal also contains the text of the preamble and resolutions of the International Health Conference held in New York in June 1946.

* * *

Another new south american medical periodical is the *Revista de Nutrición* published by the Instituto General de Salubridad, Lima, Peru, of which volume I, no. 1, July 1946, has recently been received. The journal will concern itself chiefly with the urgent dietetic and nutritional problems in Peru, but it will also include articles of wider scope as space permits.

This number contains articles dealing with the problem of the scarcity of animal protein in Peru, muscular output in relation to nutrition, the nutritional value of foods in relation to price, and an analysis of the composition and nutritional value of ices consumed in Lima during the summer of 1945.

V. E. C. M.

1043

NOTES ON OTHER JOURNALS

In April of this year Sir Alexander Fleming paid a visit to Austria under the auspices of the British Council, and lectured in Vienna on 21 and 22 April. In anticipation of this event, the *Wiener klinische Wochenschrift* published on 18 April a *Festnummer* (volume 59, no. 15) dedicated to Sir Alexander Fleming. The number opens with a greeting to Sir Alexander by the editor, Professor L. Arzt. The remainder of the number consists of original articles on the following subjects: Bacteriological experiences with penicillin (Prof. H. Chiari); use of penicillin in surgery (Prof. L. Schonbauer); use of penicillin in internal medicine (Dr. E. Lauda); chemotherapy in laryngo-rhinology (Prof. C. Wiethe); the penicillin treatment of acute osteomyelitis (Dr. A. Winkelbauer); opthalmological experiences with penicillin (Dr. K. Hruby); use of penicillin powder in Thiersch grafts (Dr. S. Tappeiner); and treatment of gonorrhoea with penicillin (Prof. L. Arzt, Dr. H. Gabriel, and Dr. W. Hofbauer).

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We have been pleased to receive volume I, no. 1, September 1946, of the *Medical Journal of Malaya*, which is the reappearance under a shorter title of the *Journal of the Malaya Branch of the British Medical Association*. This is the first number to appear since the japanese occupation. As the majority of the Association's members had been cut off from all news of medical advances for four years, the opportunity has been taken in the first few numbers of the journal to reprint certain articles which have already appeared elsewhere. These contain for the most part summaries of recent advances in particular fields, and in this number six such articles have been reprinted from the *British Medical Bulletin*. The *Medical Journal of Malaya*, which is the official organ of the Malaya Branch of the British Medical Association, is edited by Professor G. V. Allen, the business manager and publisher is C. F. Young, Post Box 664, Singapore, and it is to appear quarterly.

* * *

The aim of *International Medical Abstracts and Reviews*, a new periodical published monthly in Calcutta, is to make available to the indian medical profession all worthwhile recent medical literature. To this end it is divided into sections consisting of reviews of medical progress, abstracts of current literature, current comments, laboratory and therapeutic notes, reports of societies, book-reviews and lists of the contents of the chief medical periodicals. This journal is more attractively produced and better printed than the majority of indian medical periodicals that we have seen.

* * *

We have received for the first time a copy of *Revista Ibys* (Madrid), vol. 4, no. 7, December 1946, containing three articles dealing respectively with the acute intoxication caused by barbiturates, anaemia in pregnancy and vaccination against whooping cough. A book-review section is also included.

Historical Notes

1044

THE CAMBRIDGE MEDICAL SCHOOL

It is sad to think that the recently published book, *Some chapters in Cambridge medical history*[1], is the last which will come from the pen of Sir Walter Langdon-Brown, who died on 3 October, 1946, a short time after its publication. The book is a reprint of six papers read to the section of the history of medicine of the Royal Society of Medicine and published in the *Proceedings* of that society at various times during the last ten years. In addition, a paper first published in *Nature* forms one chapter.

The book is written with the authority of one who received his education at Cambridge and who, more than forty years later, returned there to become Regius professor of physic. Langdon-Brown was proud of his association with a school of medicine which had produced such illustrious men as John Caius, William Gilbert, Harvey, Glisson, Heberden, Paget, Humphry, Foster and Allbutt. He writes of the work of these and many others who made so great a contribution to medicine and added so much to the reputation of the Cambridge Medical School.

In his first chapter, the writer deals with John Caius and his part in the revival of learning at Cambridge. There is a lucid account of Caius, who first introduced the study of practical anatomy into the British Isles, and who was the first to teach it. It is said that Caius was a man afraid of personal relationships and that his only intimate friend was Conrad Gesner, but he gave his heart to his college at Cambridge and to the Royal College of Physicians, of which he was president in 1555–60, 1562–63, and 1571. Caius wrote an original account of the sweating-sickness in 1552.

[1] [For title, particulars and price, see *Book Reviews*.]

The second chapter concerns William Gilbert, the physician and physicist and "the first of English modern scientists". Francis Glisson is the subject of the next chapter, in which the author also deals with what he calls (after Singer) the "insurgent century", the period from the defeat of the Spanish Armada to 1688, the dawn of the "age of reason". Glisson is well known for his treatise on rickets (1650), was Regius professor of physic at Cambridge from 1636–77, was one of the original members of the Royal Society, and was president of the Royal College of Physicians. He is eponymized in "Glisson's capsule", of which he gave an accurate description in 1654.

During the next century, the chair of physic was held from 1700–41 by Christopher Green, and from 1741–93 by Russell Plumptre, both distinguished only for the length of their respective tenures of the chair. During this period, however, Addenbrooke's Hospital was founded and certain laboratories were established. In 1724, William Heberden, who was to become the most famous figure in eighteenth-century Cambridge medicine, entered St. John's College. Heberden's first printed work, *Antitheriaka*, exposed the ridiculous polypharmacy existing at that time; he also undertook with Plumptre's father a revision of the *London Pharmacopoeia*, from which he succeeded in deleting many useless (and a few useful) drugs. It is strange, as the author remarks, that Heberden was never given the chair of physic at Cambridge. He had a most distinguished career and was a friend of numerous eminent contemporaries, among them Samuel Johnson and William Cowper. The rebirth of medicine at Cambridge, which might have followed Heberden's appointment to the professorship, waited until the next century and the coming of John Haviland, George Paget, George Humphry and Michael Foster. The disciples of the last three, "the great triumvirate", are almost contemporaries—J. N. Langley, W. H. Gaskell, W. H. R. Rivers, C. S. Myers, Dew-Smith, Gowland Hopkins, Charles Roy, Sims Woodhead and A. E. Shipley, to name but a few.

In his closing chapter the writer describes the transition from the nineteenth to the twentieth century and the coming of Clifford Allbutt. Langdon-Brown must have known Allbutt intimately; he devotes a good deal of space to biographical and other information about him, and perhaps rightly, for no one could more appropriately be chosen to close this fascinating little book than Allbutt, whom Osler affectionately called "my brother Regius". Like Allbutt, Langdon-Brown attained a high literary standard in his published work, well exemplified in the present publication. It will form a most valuable supplement to the *History of the Cambridge Medical School*, written by his contemporary at Cambridge, Sir Humphry Rolleston.

L. T. Morton

1045

JONATHAN HUTCHINSON

"The Only Generalized Specialist"

While in the earlier period of the history of the Society of Friends its members were debarred by their religious beliefs from entering the other learned professions, medicine seemed to be peculiarly congenial to Quaker doctrine and practice. Thus it happened that an unusually large proportion of Friends became physicians, and the tradition, once established, persisted. In the eighteenth century Fothergill and Lettsom, in the nineteenth Hodgkin and Lister, are honoured names in medical history. Jonathan Hutchinson, the subject of a new biography[1], is fully worthy to take his place beside them. He was a general surgeon, an ophthalmologist, a neurologist, a dermatologist, a syphilologist and a leprologist, while as an observer of all kinds of rare manifestations of disease he had no equal. This versatility earned him from Professor Herkheimer of Frankfurt the description "a specialist in all medicine", and the same idea was expressed by Sir William Osler in the words "He is the only generalized specialist which the profession has produced". His main medical interest, however, was syphilis, and in the course of his practice he saw a vast number of patients suffering from this disease. "Hutchinson's triad", the syndrome of diffuse interstitial keratitis, labyrinthine disease and Hutchinson's teeth, seen in congenital syphilis, is known to every medical student. Well-known, too, is the hypothesis, which he held firmly to the end of his life, that leprosy is caused by the eating of decayed fish.

[1] [For title, particulars and price, see *Book Reviews*.]

SIR JONATHAN HUTCHINSON 1828-1913

Wellcome Historical Medical Museum

The author of this life, one of Hutchinson's sons, is not a medical man and, while giving due place to what was after all his father's main work, he has wisely refrained from going too deeply into it, in order to leave adequate space for other sides of his life, in particular the religious and the educational. While he remained all his life a faithful member of the Society of Friends and was of a deeply religious nature, Hutchinson was far from orthodox in his views. At the age of eighteen he was admonished by his father on the subject of dress with especial reference to a new and "unfriendly" hat, and he writes in his diary that day,

> "having thought much, and I believe, seriously, on the subject, my deliberate conclusion is, that the peculiarities of Friends with regard to dress and language are a piece of the most absurd folly ever intermingled with the religious system of any Christian sect".

Nevertheless in his letters to his wife, selections from which form one of the most interesting parts of this book, he always uses the "thee" and "thou" in the ungrammatical, but typical, Quaker way. Darwin's theory of evolution exerted a profound influence on his religious thought and he came to abandon the belief both in a personal deity and in a personal celestial immortality.

Hutchinson was a great teacher, and this book does full justice to this side of his life. His interest in education is shown quite early by a passage in his diary written at the age of eighteen. Commenting on a lecture on ragged-schools in which the lecturer had recommended coeducation, young Hutchinson writes:

> "I fully believe that the fair sex were intended as our companions and civilizers in childhood, as well as in more advanced life; that female companionship and sympathy are, in all ages and ranks, elevating to the character of the men."

In his advocacy of the state feeding of elementary-school children he was ahead of his time, for, in spite of the opposition of his friends, who were shocked at his "communism", he publicly recommended the provision of one good meal at least, provided out of school funds, for all children whom the state compelled to attend school.

Hutchinson was a great believer in visual aids to education, both medical and general. He founded educational museums at Haslemere and at Selby, and a clinical museum at Park Crescent, Regent's Park, later transferred to Chenies Street, off Gower Street. The Haslemere Museum remains to this day, but the medical collection was acquired after his death by the Johns

Hopkins Medical School and was thus lost to England. At Haslemere and Selby, Hutchinson gave lectures nearly every week, over a period of some twenty years, on a great variety of subjects. Love of poetry played a great part in his life, among his favourites being Wordsworth, Cowper, the two Brownings and George Herbert.

The arrangement of the material in this biography leaves something to be desired. It is neither strictly chronological nor, as the chapter-headings suggest, altogether topical. The result is a little confusing and makes it difficult to get a complete picture of any particular aspect of Hutchinson's life without referring to a great many different places in the book, nor does the somewhat inadequate index offer as much help in this respect as it should. But it would be ungrateful to end on a note of criticism, and we would rather close with these words from Mr. Johnston Abraham's foreword:

> ". . . this biography is . . . important, and . . . it is necessary it should be given to the world; for it presents a new and rounded picture of the man behind the world-famous figure; and it makes one understand why he should have asked to have carved on his tombstone the words:—
> 'A man of Hope and Forward-looking Mind.'"

Cyril C. Barnard

1046

ANTONIO SCARPA 1752-1832

Reference to histories of medicine and biographical dictionaries reveals a wide divergence of opinion as to the date of birth of Antonio Scarpa. If the date so often quoted, 13 June, 1747, were correct, this year would be the bicentenary of his birth, but in this account of his life and work the opportunity must be taken to correct an error which has long been perpetuated. As long ago as 1832 Luigi Scarenzio gave Scarpa's date of birth as 19 May, 1752, and researches made by Favaro (1932) proved this to be correct. Capparoni (1932) has explained how the erroneous date of 1747 came to be accepted: a brother born in 1747, and who died before the subject of this note was born, had been baptized Antonio. The same christian name was bestowed on the boy born in 1752 at Motta, a village in austrian Italy.

ANTONIO SCARPA 1752-1832

Wellcome Historical Medical Museum

Of poor parentage, Scarpa owed his education to an uncle, who instructed him in languages and mathematics, and sent him to the University of Padua, where he graduated Doctor of Medicine. Here he gained valuable experience while acting as secretary to Morgagni, whose failing eyesight made him depend on the young man, who dealt with his correspondence and read to him.

In 1772 his work brought him to the notice of the Duke of Modena, who appointed him to the chair of anatomy and theoretical medicine at the University of Modena, and erected a new institute for his researches. By the bounty of the Duke he spent the years 1780–81 in Paris and London, where he enjoyed the privilege of working with Percival Pott and the two Hunters. The year 1783 saw his translation to the University of Pavia, where, by the good offices of the Emperor Joseph II, he became professor of anatomy, occupying in addition the chair of surgery in 1787.

During the war between Austria and France, Scarpa was sent for by the Emperor Francis I, whose wife was suffering from a malignant disease. Under a flag of truce he crossed the Tyrol, then the seat of war, receiving a safe conduct over the frontier. The French proclamation of the Transpadane Republic in 1796 threatened Scarpa's career for, on his refusal to take the oath of allegiance, he was expelled from office. In 1805, however, Napoleon passed through Pavia on his way to Milan for his coronation as king of Italy. Received by the Faculty, he enquired for Scarpa, and on hearing the reason for his absence, ordered his immediate reinstatement, and conferred on him the grand cross of the Legion of Honour, together with a purse of 4,000 francs. Scarpa continued to hold the chair of surgery until 1812, and was rector of the Faculty until his death on 31 October, 1832. His connexion with the University thus extended from 1783 to 1832.

Endowed with a great capacity for work, he made good use of the scope which Pavia provided for anatomical research, and had a lucrative private practice. Scarpa's fascia, foramen, membrane, shoe and triangle are eponyms known to every medical student. Though he is rightly regarded as a great anatomist, his work covered a much wider field than is generally realized. His first work to win recognition was *De structura fenestrae rotundae auris et de tympano secundario anatomicae observationes*, Modena, 1772. (Sir Benjamin Ward Richardson was apparently unacquainted with this edition, for in his study of Scarpa he states that the book was published some time after 1789.)

In 1794 appeared his work on the nerves of the heart, *Tabulae neurologicae, ad illustrandam historiam anatomicam cardiacorum nervorum*, Ticini, which was highly praised for its correct delineation of the nerves and for the excellence of the anatomical plates. *Saggio di osservazioni e d'esperienze sulle principali malattie degli occhi*, Pavia, 1801, was translated into English in 1806. During his enforced "vacation" he had studied the subject of clubfoot, for which he designed a shoe which has served as a model for makers up to recent times. In addition, he had brought out the above-mentioned work on the eye, in which he contended that surgery of the eye was a part of general surgery. He was responsible for the revival of the old operation for cataract by depression, as opposed to extraction. Whilst operating for cataract on one occasion, the straight needle he was using, being poorly tempered, became bent, and, undeterred by this accident, he perceived the advantages of the curved instrument, which he used for all future operations of this nature.

Of Scarpa's works on hernia, the first, *Sull' ernie. Memorie anatomico-chirurgiche*, Milano, 1809, was popular for many years and often translated. As a supplement, he published *Sull' ernia del perineo*, Pavia, 1821, wherein he proved that hernia through the perineum was possible. This had often been questioned, but Scarpa, who had designed a truss for a patient with perineal hernia, had, on his death by other causes, conducted a post-mortem to verify his opinion.

Space forbids a description of all the works of Scarpa. It must suffice to say that his work on scirrhus and cancer (*Sullo scirro e sul cancro*, Pavia, 1825) embodies much that would command respect at the present day. In addition to the works mentioned, Scarpa contributed a number of books which have enriched medical literature: *Anatomicae disquisitiones de auditu et olfactu*, Ticini, 1789; *Depenitiori ossium structura commentarius*, Lipsiae, 1799; *Sull' aneurisma, riflessioni ed osservazioni anatomicochirurgiche*, Pavia, 1804; *Memoria sulla legatura delle principali arterie degli arti*, Pavia, 1817; *Saggio di osservazioni sul taglio rettovescicale per l'estrazione della pietra dalla vescica*

orinaria, Pavia, 1823; *Memoria sull' idrocele del cordone spermatico*, Pavia, 1823.

Held in high esteem by british scientific men, Scarpa was elected a Fellow of the Royal Society in 1791.

T. H. Bishop

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1047

CENTENARY OF THE DEATH OF G. M. BURROWS 1771-1846

The centenary of the death of an interesting figure in the history of general practice, and a leading authority on insanity in his day, fell on 29 October, 1946. Born in 1771 at Chalk, near Gravesend, George Man Burrows received his education at King's School, Canterbury, from which he was apprenticed, in his sixteenth year, to a surgeon-apothecary of Rochester named Richard Thompson. Dr. Burrows qualified at the College of Surgeons and the Society of Apothecaries after completing his medical education at Guy's and St. Thomas's Hospitals. After qualifying he became a general practitioner in London, and soon began to devote his energies to raising the status of the doctor engaged in general practice. He was instrumental in forming the Association of Surgeon-Apothecaries of England and Wales "to improve the education and render more respectable their own body" as a means to this end (Munk, 1878). For three years he acted as chairman of the Association and, largely as a result of its work, the Apothecaries Act[1] was passed in 1815. Its work accomplished, the Association dissolved, but not before it had voted 500 guineas to Dr. Burrows in recognition of his labours.

After the passing of the Act, a Court of Examiners was formed by the Society of Apothecaries, of which Dr. Burrows was a member until a dispute arose over the conduct of the Court of Assistants. He accordingly resigned early in 1817, and published a *Statement of circumstances connected with the Apothecaries Act and its administration*. But the first great task of his life was accomplished. As a result of the passing of the Act, adequate machinery had been established for testing the knowledge of candidates for general medical practice, and the status of the general practitioner had been raised accordingly. The qualification granted from Apothecaries Hall was to hold the field until the Royal Colleges instituted the conjoint examinations later in the century.

The second part of the life of G. M. Burrows began when he gave up general practice in 1816 and turned to the treatment of insanity. Commencing modestly with a small mental home at Chelsea, he opened a larger establishment, called the "Retreat", at Clapham in 1823. He obtained the diplomas of M.D. St. Andrews and L.R.C.P. London, in the following year, and was admitted a Fellow of the Royal College of Physicians in 1839. On 29 October, 1846, he died in his seventy-sixth year and was laid to rest in Highgate cemetery. These are the bare facts, but during this period of his life Dr. Burrows had become a leading practitioner in his speciality and written two books that had added to his reputation.

The literary activities of Dr. Burrows were considerable. He was one of the founders and editors of the *London Medical Repository*, which commenced publication in 1814 and quickly became established. It was in this journal that he published "Observations on the comparative mortality of Paris and London", which was intended to dispel the impression overseas that the British were "most devoted to the practice of suicide". In the same year, 1815, he wrote "An account of two cases of death from eating mussels, with some general observations on fish-poison."

Impressed by the fact that "no detailed or even general report of the result of private practice in this malady [insanity] has ever been published by any British author" (Burrows, 1820), he decided to write his own *Commentaries*. Many years' delay in the appearance of this work caused the author to issue in advance *An inquiry into certain errors relative to insanity; and their consequences; physical, moral, and civil*, 1820, with the object of discounting certain popular errors of the time, e.g., that insanity was incurable. This book contains an interesting passage on private charity versus state enterprise:

> "In the evolution of futurity, events are unfolded that justify a departure from established and approved customs. Hitherto it has been our glory and boast, that while, in foreign countries, every plan promotive of benevolence, science, or the arts, emanated from the government, and was always at the charge of the public; in the British empire those objects were accomplished by the spirit and liberality of the community. And when this feeling ceases to operate, the enviable superiority our institutions have attained, must decline, and no longer preserve their present general pre-eminence. If, however, a deviation from so exalted a principle be ever permitted, I conceive it may in respect to the civil regulation of lunatics."

The *Commentaries on the causes, forms, symptoms, and treatment, moral and medical, of insanity* was published in 1828, and was quickly recognized as the best work on its subject. Dr. Burrows was far-sighted enough to see that the treatment of insanity had an optimistic future. Even in these days when modern methods of treatment seem to be adding to the number of cures it may still be said: "The utmost success hitherto recorded falls short of that which is attainable" (Burrows, 1820).

F. Tubbs

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[1] [In the course of the 18th century, the apothecaries became recognized in England as general medical practitioners. The Apothecaries Act formally confirmed their status in this capacity.—ED.]

1048

JOHN ATKINS: AN EIGHTEENTH-CENTURY NAVAL SURGEON

Among the eighteenth-century naval surgeons who do not deserve to fall into oblivion may be numbered John Atkins. At a time when their importance was not generally recognized, he advocated cleanliness and fresh air in the prevention of disease. A competent observer, he embodied the results of his surgical experiences in a volume entitled the *Navy surgeon*, 1732. Born in 1685, Atkins entered the navy after completing his surgical apprenticeship (Moore, 1885) and was present at Sir George Rooke's naval engagement with the French on 13 August, 1704. It was a drawn fight, but casualties were heavy and Atkins was not without patients. There was Alexander Henderson who had his left eye struck out by a splinter, and Thomas Gibbs who received a large gunshot wound behind the neck. Gibbs lay for dead and would have been thrown overboard had not his gunmates perceived some small signs of life in him (Atkins, 1737).

In 1707 Atkins was aboard the *Tartar* stationed in the Channel.

> "We now and then", he says, "used to . . . make little southerly excursions, in hope of a prize; or to meet the Dutch vessels from Bourdeaux, who being our good friends and allies, we made to traffic with at pretty cheap rates."

On one of these occasions the *Tartar* narrowly escaped capture, only escaping under the cover of darkness. One of the crew, however, received a musket-shot through the thorax, and Atkins gives a detailed report of the case, observing that gun-shot wounds are "less dangerous, if they do not hit on large vessels, than wounds made by sharp instruments." (Atkins, 1737.)

Three years later Atkins was serving on the *Lion*. The fleet under the command of Sir John Norris lay in Vaia Bay near Genoa in March, 1710, when two enemy ships were sighted. The *Lion* in company with the *Severn* and the *Lime* gave chase. In the ensuing action forty men were wounded including the *Lion's* captain, Galfridus Walpole, whose right arm had to be amputated above the elbow. Atkins was called upon to amputate a number of shattered limbs, and in his account of his patients makes an observation that is of interest to all who have wondered

how naval surgeons chose their time to operate in the pre-anaesthetic era. He writes:

> "The heat and surprize in action makes it the properest time for amputating, men meeting their misfortune with greater strength and resolution, than when they have spent a night under thought and reflection."

In February, 1721, Atkins sailed for the Guinea Coast with the *Swallow* and the *Weymouth*, commissioned to suppress piracy off the west coast of Africa. The voyage was attended with some success, for two hundred and seventy pirates were captured at Cape Lopez with ten thousand pounds in gold-dust. But sickness proved a greater enemy than pirates. Three or four of the crew died every day for six weeks and Atkins had to act as purser for want of any other suitable survivor (Moore, 1885). After sailing to Brazil and the West Indies, where at Port Royal a hurricane carried off the masts, he returned to England in April, 1723.

Atkins was apparently ambitious. In his account of Captain Walpole's case he records that he suggested that

> "two or three of our skilfullest surgeons" be called in consultation "not only as a duty to a gentleman of his [Walpole's] distinction, but a distant view, that the care and reputation which might accrue to me by their assistance in the cure might possibly place a man in one of the King's Yards".

But the shore appointment did not materialize. He was well read in the literature of his day, and perhaps had read in the *Dispensary*, by his contemporary, Dr. Samuel Garth,

> "Who wants not merit needs not arm for fame;
> The dead I raise my chivalry proclaim
> Diseases baffled, and lost health restored
> In fame's bright list my victories record".

Atkins turned to the pen. In 1732 the *Navy surgeon* first appeared and was sufficiently popular to be reissued in an abridged form. His experiences in the tropics provided the material for *A Voyage to Guinea, Brazil and the West Indies* . . . 1735, in which he describes the slave trade. A curious little pamphlet entitled *Observations on the coast of Guiney* was issued as an appendix to the *Navy surgeon*. It deals with such subjects as the climate, the colour of the natives, and prevalent diseases. He advocates fresh air in sickrooms (cabins), and in extolling the virtues of cleanliness and good ventilation writes that the crew should

> "have as free and frequent communication with the fresh air (by opening the ports) as may be consistent with safety and their other affairs, points too much overlooked and disregarded, though of the greatest consequence to preserve a ship's company on a voyage."

The last edition of the *Navy Surgeon* was published in 1742, but nothing more is known of Atkins's activities. He died in 1757 (Moore, 1885).

F. Tubbs

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1049

JOHN AND WILLIAM HUNTER

A new scholarly book[1] on John and William Hunter, by Miss Oppenheimer, contains two independent essays, of which the first is much the more important. It is a defence of Everard Home, who was John Hunter's assistant, brother-in-law and executor, for his rash destruction of Hunter's unpublished papers thirty years after Hunter's death. Miss Oppenheimer has studied Home's career in detail and her essay is precisely documented with notes and references and a bibliography of Home's numerous publications; it would be valuable for this careful detail alone. It is also an incentive to Hunter's admirers to compare his achievement with Home's and, in the light of Miss Oppenheimer's evidence, to decide whether Home deserves the obloquy which has pursued him since his burning of the books, or whether this was not made an occasion, as Miss Oppenheimer concludes, for spiteful denigration by William Clift, Hunter's last secretary and the conservator of his museum. Her conclusion is weakened by two misapprehensions. Firstly, she seems to accept Benjamin Brodie's remark that he had seen Hunter's papers at Home's house and that they were rough notes useless since Hunter's death. This opinion is more than doubtful in view of what was gleaned from Hunter's surviving papers by Clift and Richard Owen. Also it does not square with the supplementary defence of Home that he had by 1823 published all that was of value in Hunter's notes, with due acknowledgement. Secondly, she misjudges Clift's character and underestimates his ability. Those who take the orthodox view will not be shaken by Miss Oppenheimer, but must study her evidence before maintaining their bad opinion of Home.

The essay on William Hunter, less important and not controversial, will appeal more readily to the general reader of medical history. It is based on a wide knowledge of the memoirs of the period, and brings out extremely well an aspect of Dr. William that has not been fully described before, his relations with patients and friends in the world of literature and politics. His hypersensitive quarrelsomeness, so unlike John's blunt forthrightness, appears markedly in this new sketch. It is strange to learn that he, who broke with his brother, kept a lasting friendship in spite of temporary differences with another pernickety old bachelor, Horace Walpole.

W. R. L.

[At a generous estimate this book contains 40,000 words. It consists of two distinct essays, of a style and length suitable for publication in one of the journals devoted to medical history. The price of these essays bound as a book is such as to discourage most private purchasers.—ED.]

[1] [For title, particulars and price, see *Book Reviews*.]

Book Reviews

The prices quoted are those which obtain within the United Kingdom

ANAESTHESIA

1050 Physics for the Anaesthetist

R. R. Macintosh & W. W. Mushin. Oxford, Blackwell Scientific Publications, Ltd., 1946. vii + 235 pages; 282 figures. 22 x 14 cm. £1 10s. [£1.5]

(i) Molecular movement: molecular weight: Avogadro's hypothesis: density: the Waller chloroform balance: Clover's chloroform apparatus; (ii) heat: specific heat; (iii) vaporization: latent heat of vaporization; (iv) laboratory experiments; (v) heat loss during anaesthesia; (vi) latent heat of crystallization; (vii) partial pressure; (viii) vapour pressure; (ix) atmospheric pressure: ether vapour pressure: respiration at high altitudes; (x) vapour and gas: nitrous oxide cylinder pressure: specific volume: Boyle's Law: isotherm: filling ratio: Charles' Law: Gay-Lussac's Law; (xi) flow of fluids through tubes: Poiseuille's Law; (xii) laminar and turbulent flow: resistance of anaesthetic apparatus; (xiii) flow of fluids through orifices; (xiv) flowmeters; (xv) the injector and its applications; (xvi) solution of gases: tension of a gas: oxygen therapy; (xvii) diffusion of gases and liquids: Fick's Law: osmosis: filtration: pulmonary oedema: respiratory obstruction; (xviii) development of anaesthetic apparatus: ether vaporizers: physical data: conversion factors. Biographical notes. Index.

This is a timely and useful book for which anaesthetists have increasingly been feeling the need. In it will be found the answer to many questions which the anaesthetist may ask himself, or may—sometimes to his embarrassment—have put to him.

The book's chief fault is over-simplification. The numerical data are given to two significant figures, so that the product of 28 and 63 is given as 1800 (p. 26), and the result of a simple calculation coming to 165 calories is given as 160 (p. 49). Figures for physical constants are frequently given for non-standard—and unstated—conditions; and some of the experiments are dangerously oversimplified. In an example showing how to correct the volume of a gas for change of temperature and pressure, the correction for pressure is wrongly applied (p. 109). Physics is an exact science, and a book on physics containing errors of this magnitude may fail to win the reader's confidence, and falls short of the standard of accuracy to which the modern anaesthetist should aspire. The authors "disclaim any pretence at being physicists", but this should not be used as an excuse for laxity, especially as the help of a physicist was available, and is freely acknowledged in the book.

The authors have, however, done a great service in bringing together a mass of most useful information. The sections on vapour-pressure (with a valuable composite graph), fluid-flow, and flowmeters are admirably clear; and some popular misconceptions, such as those on warmed gases, are convincingly exploded. The effect of the calibre of syringes, needles and endotracheal tubes on the passage of fluid through them is well brought out, and its practical application is emphasized.

The phenomena of vaporization, and of specific heat and heat-transfer are well expounded; and partial and reduced pressure, diffusion, osmosis and filtration are clearly explained. There is an informative section on the filling of cylinders and the behaviour of their contents.

At the end of the book is a comprehensive table of physical data. This provides much useful information which the scientific anaesthetist constantly needs, but has never before had conveniently provided.

It is a pity that space could not have been found for a chapter on the ignition of anaesthetic gases and vapours.

The book is well arranged and attractively produced; and Miss McLarty's illustrations and diagrams are so clear as to be self-explanatory.

1051 A Short Handbook of Practical Anaesthetics

Höel Parry-Price. Bristol, John Wright & Sons Ltd., 1946. 127 pages; 50 figures. 19 x 12 cm. 12s. 6d. [£0.625]

(i) Introductory; (ii) instructions on anaesthetics for the nursing staff: (iii) general anaesthesia and some of its difficulties; (iv) gas-oxygen and gas-oxygen-ether; (v) cyclopropane, ether, and endotracheal anaesthesia; (vi) intravenous and local anaesthesia; (vii) anaesthetics for special operations; (viii) gases used for respiratory support and drugs for premedication; (ix) carbon-dioxide absorption apparatus; (x) dangers, accidents, and complications of anaesthesia; (xi) falls of blood-pressure occurring during anaesthesia; (xii) the variations between service and civilian anaesthetics. Conclusion. Index.

This little book is clearly a wartime product. It is composed partly of material written for the information of naval sick-berth attendants, and much of it is written from the point of view of the anaesthetist in the armed forces. A wide range of good material is compressed into very small compass, so that the treatment is somewhat patchy. The style is conversational, wandering, and sometimes careless. It is illustrated with a few well-chosen anecdotes, which point their moral very tellingly.

Much is made of the need for asepsis in lumbar puncture, but nothing is said about wearing gloves. The author would have us believe that "absolute relaxation can be obtained by cautious whiffs of ether" added to gas-and-oxygen when the intestines are being handled; and that the use of an intratracheal tube *prevents* the introduction of septic material from the nose and throat into the lung. We are told that the patient should be carefully examined when he arrives in the anaesthetic room. This is clearly preferable to no examination, but most anaesthetists feel that a better place and time should be chosen for it. Published work is frequently mentioned, but in no instance is a proper reference given.

The nursing staff and the young anaesthetist will find much of value in the book, and particularly in the section on "anaesthetic tips", which contains a wealth of useful information.

The reproduction and the paper are good, but 12s. 6d. seems an unduly high price for so slight a work.

BIOLOGY

1052 Spuren von Stoffen Entscheiden über unser Schicksal

Emil Abderhalden. 2. Auflage. Basel, Benno Schwabe & Co., 1946. 106 pages; 62 figures. Sw. fr. 6.

This short book is addressed mainly to the lay reader, yet accuracy is not sacrificed to popularity of presentation. The underlying theme, expressed in the title, is developed by a description of the nature and roles of hormones, vitamins, mineral salts, enzymes and antibodies. There is a clear account of the mode of working of the autonomic nervous system, and the mutual interaction of the endocrines and their role in the body. The intricate subjects of intermediate metabolism and intracellular processes are dealt with lucidly. The customary analogy of the cell to a chemical factory is rejected on the grounds that the very substance of each cell is in continual flux. "Metabolism is governed by dynamics, not by statics". The "burning of food" in the body is explained by an account of the complicated oxidation- and reduction-processes by which the gradual release of energy from complex molecules is achieved.

Professor Abderhalden does not confine his discussion to the animal world, but shows how, by the agency of plant and bacterial enzymes, inorganic molecules are made available for utilization by animals, so that the continuity of life is assured. "The whole tremendous process of the mutual relations between plants and animals is governed by enzymes". The development of each subject is traced with special emphasis on the fruitful co-operation between scientists of various disciplines, and the present trend of research is indicated together with its practical significance. Excellent photographs illustrate some methods of hormone and vitamin research. This stimulating book can be recommended not only to the interested general reader, but also to those engaged in research and teaching.

I. J. L.

1053 Biology of Tissue Cells. Essays

Albert Fischer. Cambridge, University Press, 1946. 348 pages; 55 figures. 24 x 16 cm. £1 11s. 6d. [£1.575]

(i) Units of living matter; (ii) tissue cells in vivo and in vitro; (iii) general morphology of tissue cells in vitro; (iv) special morphology of tissue cells in vitro; (v) rate of growth; (vi) tissue culture as a whole; (vii) regeneration; (viii) differentiation and organization; (ix) interchange of cells and medium. (Senescence and rejuvenescense); (x) the nature of the growth-promoting substances; (xi) nitrogen metabolism of tissue cells; (xii) energy exchange of tissue cells cultivated in vitro; (xiii) concluding remarks and perspectives. Index.

This book on the biology of tissue cells is mainly concerned with specifically biological problems, such as cell-morphology, ecology, differentiation, and the concept of an organism. Penetrating into these are biochemical and biophysical discussions. The morphology, etc., makes fascinating reading; the biochemistry, if not far-reaching, is sound; the biophysics is not above reproach. In these respects Dr. Fischer has reflected the best that is available in these fields. For example, in Britain there are many teaching and research departments of biology with a fine and well-established tradition: departments of biochemistry are well-established but comparatively new; it is too early to predict how far-reaching will be the influence of biochemistry on biology as a whole: and as yet there is not a single teaching department of biophysics; biophysics is still in its infancy. The situation in other countries in general, and in Denmark in particular, is not dissimilar. A further hall-mark indicative of the hand of a distinguished research worker is that each chapter, perhaps each page, leads on to further research. There is as much, or more, interest in the growing points as in the established facts. This is in consequence an indispensable book for those interested in cells and in tissues.

Although it covers so wide a field, this book is not intended to be an exhaustive treatise on tissue culture. It is a series of essays on the general physiology and biology of tissue-culture cells in their relation to organisms. The general problem of the relation of the cell to the organism is the main theme of the book. Much evidence is adduced to show that cells in tissue culture do not grow and behave as isolated individuals, but in a manner suggesting that an avian or mammalian tissue-culture is an organism, possibly of a very low order, but still an organism. For a culture cannot, as with protozoa, be grown from a single cell: there must be a number of cells in the original implant. Again, a culture shows marked differentiation of cells, according to their position in the culture, the nature of the environment, and the age of the culture. This Dr. Fischer attributes partly to the gradients of metabolic products in which the cells find themselves. But it must be emphasized that the cells do not react to these gradients by migrating until all cells have the same environment. Instead, the culture reacts rather as an organism, reaching a size which is to a marked degree a fraction of the original implant, and, if injured, repairing the injured region rather than growing as a whole.

The final fifth of the book is devoted to the nutritional requirements of tissue-culture cells. In this difficult field relatively little advance is recorded; this part of the book is by far the least satisfying. One hopes that more attention will be given to this very important problem.

J. F. Danielli

1054 Genetics for Medical Students

E. B. Ford. London, Methuen & Co. Ltd., 1946. 163 pages; 10 figures. 18 x 12 cm. 7s. 6d. [£0.375]

(i) Mendelian heredity; (ii) the genetics of sex; (iii) mutation and the nature of heredity; (iv) the action of the genes; (v) polymorphism; (vi) methods of study in human genetics. Appendix. Bibliography. References. Index.

That a second edition of this book should appear so shortly after its initial publication is in itself, especially in these times, a testimony to its proven usefulness. For such a book as this there is undoubtedly great need, since an introduction to genetics is being offered in all medical schools both in undergraduate and postgraduate courses. It so happens that at the moment this book of Dr. Ford's is the only one which is available. It therefore must exert a very considerable influence upon the attitude of the members of the medical profession in general towards the subject of genetics.

The book had its origin in courses of lectures given by the author to medical students and it hence reveals the ideas of the author concerning the placing of emphasis among the different topics that are considered. There can be no hesitation in recommending this book as a textbook for such as are attending courses of instruction in human and clinical genetics. This edition differs from the first only in respect of a few minor changes and the addition of an appendix devoted to the Rhesus antigens. Since this story is as yet unfinished, it may be that Dr. Ford is wise in dealing with it in a somewhat superficial manner.

It so happens that those of us who have been teaching this subject have in recent years been recommending to our students that they should get one of two books, whichever happened to be available—this one by Dr. Ford, and Dr. J. A. Fraser Roberts' *Introduction to medical genetics*. They deal with the same subject, cover the same ground and are addressed to the very same group. The first has been used by some, the second by others, and it has been interesting and indeed helpful to collect the views of members of medical postgraduate classes concerning the relative usefulness of the two. It would seem that that of Dr. Fraser Roberts is strongly preferred. This is, from the point of view of production, a much better book, as it should be since it is far more expensive. Its print is most pleasing and its illustrations profuse. But it would seem that the main reasons for this preference are firstly the novel, and apparently very helpful, method of presentation of the subject-matter—a point worthy of careful consideration by all who write this kind of manual—and, secondly, the sense that the author was himself well experienced in clinical medicine. This derives, of course, from the placing of the emphasis by the author on purely clinical topics and clinical considerations.

The fact is that for certain categories of postgraduate students both books are necessary. One places the emphasis on clinical genetics and the other rather more upon population genetics. Amongst human geneticists there is some controversy concerning the wisdom of Dr. Ford in including in one of his appendices a classified list of some inherited characters in man. Since, as the author himself states, this list is not intended to be complete, it is very doubtful indeed whether it helps to provide a true measure of the importance of genetics in clinical and population medicine.

CHILD AND HOME

1055 The Problems of Family Life—An Environmental Study

Agatha H. Bowley. Edinburgh, E. & S. Livingstone Ltd., 1946. 20 plates. vii + 99 pages. 18 x 13 cm. 5s. [£0.25]

(i) The elements of happy family life; (ii) the psychological needs of the family; (iii) parents and children in difficulties: teachers and children in difficulties; (iv) anxious parents and anxious children; (v) habit disorders at home; (vi) "naughty" children. Appendices. Bibliography. Index.

Miss Bowley has an enviable opportunity, springing from her experience as a general psychologist and educationalist, and a student of family life as seen in the mirror of a Child Guidance Clinic. This enables her to see the problems of the family as a whole, so that the factors of intelligence, personal emotional structure and environmental stress can be woven together for diagnosis and remedial adjustment. Dr. Bowley wisely does not delve into the dark and tangled undergrowth of the unconscious mind to account for the problem-family. For her very thesis is an environmental study, an inspection of the interpersonal relationships of parents and children subject to common but accessible environmental stresses. She deals, for example, in the first place with the happy family of the average british home, its structure and its psychological needs. From that she naturally passes to considering the everyday problems, the unstable and neglectful parent, the rejected child, the broken home. She discusses the problems as they appear to the teacher and lays down simple and intelligible rules for the management of the nervous child. From the simple she passes to the more complex, considering defects of the anxious parent who can produce anxious children.

Some useful and simple statistics are given with regard to the distribution of such factors as intelligence-level, marital circumstances, psychological atmosphere, and her findings will be shared by all observers in this field.

1056 The Nervous Child

Hector Charles Cameron. Fifth Edition. Oxford University Press, 1946. viii + 252 pages; 8 plates. 19 x 13 cm. 10s. 6d. [£0.525]

(i) Doctors, mothers, and children; (ii) observations in the nursery; (iii) management and conduct; (iv) want of appetite and indigestion; (v) want of sleep; (vi) some other signs of nervousness; (vii) enuresis; (viii) toys, books, and amusements; (ix) nervousness in early infancy; (x) management in later childhood; (xi) nervousness in older children; (xii) nervousness and physique; (xiii) the underlying disturbances of metabolism in the nervous child; (xiv) the nervous child in sickness; (xv) nervous children and education on sexual matters; (xvi) the nervous child and school. Index.

Dr. Cameron's reputation is testified by a volume which has been held in esteem since 1919, and the fifth edition has little altered since then. This is not surprising in some respects, as the subject-matter concerns the behaviour and mental health of children, which have remained unchanged in the passage of years. The problems of child-behaviour spring from the basic emotional relationship of child and parent and, while economic changes and culture cloak and the vicissitudes of war and peace determine the surface-patterns of our conduct, the deep undertones are not subject to profound variations. Dr. Cameron is wise, therefore, in having left unchanged his description of the common problems of child-psychology.

The life of the nursery (where children are in the nursery), the common manifestation of nervousness, the developmental signs of growth, comprehension and emotional control cannot escape the acute observer of this or any generation. What really matters are the interpretations placed on conduct and the methods used in meeting and alleviating the distresses and obliquities of childhood. Furthermore, if we are to make a comprehensive study of the child in health and in phases of nervous disorder, we cannot confine our observation to the child of the well-to-do in its nursery with its trained—and perhaps overtrained—nurse, its not altogether accessible mother, and its unlimited dietetic advantages and its equally unlimited toys and cultural aids. The doctor is confronted with the child of working mothers with no nursery, no nurse, a tired husband and the bawdiness of a tenement or at best a prefabricated house. *Au fond* the problems are frequently the same, but the relationships are less complex and not obscured by the divided loyalties resulting from the presence of the nurse and the almost putative mother. To handle such problems of the elementary family needs perhaps less subtlety but more directness in the face of frequent economic and social obstacles.

Moreover, regarding interpretation, commonsense, which Dr. Cameron shows in kindly abundance, is enough to adjust many disorders of childhood, but the more recondite interpretations, which grow out of psychoanalytic theory and practice, cannot be lightly put aside. Granting the surprising emphasis which Freud places on sexuality, the instinctual life of the child viewed from an adult and not well-informed standpoint seems strange, but cannot be discounted, nor can the conflicts arising from total frustration of primitive needs be ignored. They certainly cannot be by those who observe uninhibited children at play when nurses' backs are turned and when doctors are not making their official visits.

With regard to the author's reference to the metabolic disorders, again we must refer him to the now-established trends of psychosomatic medicine. It is in childhood that we witness the foundation of metabolic troubles, and the child more than the adult is a body-mind in which emotion, growth and behaviour are inextricably interwoven. What may seem bizarre has become

commonplace to the psychiatrist who does not, as Dr. Cameron supposes, read Freud and then interpret to the child. In this respect Dr. Cameron's otherwise time-honoured book, full of wisdom in everyday observation and suggestion, is lacking in the modern insight which springs from a rational and objective child-psychiatry.

1057 The Care of Young Babies

John Gibbens. Second Edition. London, J. & A. Churchill Ltd., 1946. viii + 200 pages; 14 illustrations. 18 x 12 cm. 5s. [£0.25]

(i) Preparing for the baby; (ii) for husbands and fathers; (iii) clothes; (iv) the nursery; (v) growth and development; (vi) breast-feeding; (vii) difficulties in breast-feeding; (viii) artificial feeding; (ix) early mixed feeding; (x) feeding after the sixth month; (xi) nursery routine; (xii) the care of the skin and hair; (xiii) good muscles and sound limbs; (xiv) minor ailments; (xv) the care of twins and premature babies; (xvi) miscellaneous. Appendices. General index.

1058 Some Minor Ailments of Childhood—Being Hints to Mothers

Beryl Twyman. Edinburgh, E. & S. Livingstone Ltd., 1946. 32 pages. 18 x 12 cm. 9d. [£0.0375]

(i) Nursing and feeding sick children; (ii) independence in young children; (iii) frequent colds; (iv) poor appetite; (v) the nervous child; (vi) some hints on naughtiness and its prevention; (vii) bed-wetting and similar troubles; (viii) sleep problems.

Of books dealing with the care of infants and young children, there seems no end. That Dr. Gibbens' book, however, has met a need is shown by the fact that five reprints of the first edition have been necessary since 1940. The second edition has been thoroughly revised and deals comprehensively on more or less orthodox lines with all aspects of infant care. The opening chapters on preparing for the baby and for husbands and fathers are particularly good. In view of modern trends, particularly in the United States, one is glad to see the stress laid on the importance of breast-feeding and the clear advice given on how to overcome such difficulties as may arise.

Mothers of young children may be divided roughly into two classes—those who can read a book of this kind with profit and those who cannot. Dr. Gibbens has tried to cater for both classes, but, although he has succeeded admirably in meeting the needs of the more intelligent group, it is unlikely that mothers with a lesser degree of educational equipment would profit by its perusal even if they could afford to buy it. Indeed, it is doubtful whether any attempt to meet the needs of women of this type by means of a pamphlet is likely to succeed. Dr. Twyman has tried, but in doing so, she seems to have fallen, as it were, between two stools. In certain situations, however, it might prove useful as a supplement to individual teaching.

J. J. M.

[1028] Report of the Care of Children Committee

Cmd. 6922. London, His Majesty's Stationery Office, 1946. 195 pages. 24 x 15 cm. 3s. [£0.15]

Introduction. Section I: Existing statutory provisions and administrative arrangements. Section II: How the children are cared for now. Section III: Conclusions and recommendations. Statistical tables.

[For review, see *BMB* 1028.]

FORENSIC MEDICINE

1059 Forensic Medicine

Douglas J. A. Kerr. Fourth Edition. London, Adam & Charles Black, 1946. xii + 359 pages; 89 illustrations. 22 x 14 cm. 18s. [£0.9]

(i) Introduction—General Medical Council—professional secrecy; (ii) legal procedure in case of death; (iii) identification; (iv) changes after death; (v) death and sudden death; (vi) wounds and wounding; (vii) examination of blood and hairs; (viii) accident, suicide and murder; (ix) injuries to the head; (x) injuries to different parts of the body; (xi) burning, lightning and electric shock; (xii) gunshot wounds and identification of fire-arms; (xiii) heat, cold, starvation and neglect; (xiv) asphyxia; (xv) pregnancy, delivery, abortion; (xvi) infanticide; (xvii) sexual offences; (xviii) insanity and insane states; (xix) criminal responsibility and treatment of offenders; (xx) legal aspects of insanity; (xxi) toxicology; (xxii) mineral acids and alkalis; (xxiii) organic acids; (xxiv) metallic irritants; (xxv) irritants (cont.); (xxvi) animal and food poisoning; (xxvii) vegetable poisons; (xxviii) soporifics and antipyretics; (xxix) irrespirable gases; (xxx) miscellaneous poisons; (xxxi) civil actions. Appendix: The Poisons Rules, 1935. Index.

This well-known textbook of forensic medicine has now reached its fourth edition in some ten years, reflecting a popularity with both teacher and student which is well-deserved. It is short yet comprehensive, a model of clarity, well-reasoned, readable and reliable. The whole field of the legal, medical and toxicological aspects of the subject receives the able treatment of an author who is plainly widely-experienced in all departments and, except for a diversion on criminal responsibility, the space allotted is everywhere commensurate with the importance of the subject. The illustrations are arresting and chosen with judgement, though their relation to the text is a little haphazard owing to the greater frequency of photographs of wounds as compared with those of, say, new-born infants found in the lavatory-pan or of industrial stigmata. Good new writing has added to the attractions of the sections on blood-stains and their grouping, on the interpretation of blunt injuries to the head, and on many other smaller details. This edition also provides references for further reading at the ends of chapters. The principle is excellent but the selection has not the same merits throughout: whereas no less than ten references are given for further reading on blood, only one unimportant trifle is given for firearm-wounds and none at all for any one of the chapters in the section on toxicology—which should refer to much modern industrial work.

These are small criticisms of a book whose entire substance gives so little real cause for dissension. Douglas Kerr provides an outstanding example of clear teaching of elementary principles, a book eminently suitable for both the student and the practitioner.

Keith Simpson

FREEZE-DRYING OF PROTEINS

1060 The Preservation of Proteins by Drying with Special Reference to the Production of Dried Human Serum and Plasma for Transfusion

R. I. N. Greaves. London, His Majesty's Stationery Office, 1946. (Medical Research Council Special Report Series No. 258.) v + 54 pages; 25 illustrations. 24 x 15 cm. 2s. [£0.1]

General introduction. (i) Methods of drying; (ii) the technical aspects of freeze-drying by condensation on mechanically refrigerated condensers; (iii) the development of the apparatus used by the M.R.C. Drying Unit and a report on the work done by the Unit. Summary. Acknowledgements. References.

This report, by an acknowledged expert, is intended for the general scientific reader and may be regarded as a valuable handbook of freeze-drying. It is explained in the introduction that commercial drying-processes lead to a degree of denaturation which is excessive for biological materials, although allowable in proteins that are to be cooked for food. Biological materials must, therefore, be treated by the process of vacuum freeze-drying, which leads to little or no protein denaturation but is unfortunately far too costly to be applied to less-valuable materials.

Part I of this report gives a brief survey of commercial drying-processes, and traces the development of the freeze-drying of biological materials from the early work of Shackell (1909) to the present day. The numerous modern methods of freeze-drying are outlined, and it is shown that the vacuum-manifold and chemical dessicant must be replaced by the vacuum-chamber and mechanically-refrigerated condenser, especially where large volumes in sterile-capped bottles are to be accommodated. A discussion on the desirable condenser-temperature is confused, particularly as the author makes the tacit assumption that the rate of vapour-transfer from product to condenser is directly proportional to the vapour-pressure difference between these surfaces. Part I concludes with an interesting speculation on spray-drying from the frozen-state, and it is to be hoped that this method will be the subject of future investigation.

Part II deals with the technical aspects of freeze-drying by condensation on mechanically-refrigerated condensers. It is shown that sera will dry well if held below −10° C. in the early stages of drying, although certain samples of broth may require temperatures as low as −60° C. The operating condenser-temperature must be chosen accordingly. In all freeze-drying techniques the methods of vacuum-maintenance and measurement are of paramount importance and the sections which deal with these matters, although familiar to many, will be of interest

to the general reader. A further section explains the details of heat-control and the manner in which heat-input must be balanced against rate of vapourization. Empirical equations are given showing the approximate relationships which exist between vapour-pressure difference, obstruction to vapour-flow, and heat-input. Certain arguments in this section are invalidated by the assumption that limiting-values may be given to the variables of an empirical equation. Notwithstanding this objection, these equations appear to be of value for correlation within the experimental range. Further sections deal with temperature-measurement, sterility, dry-weight determinations, the packing of dry material, and condenser-refrigeration. Part II is concluded by a section on the freezing of protein solutions prior to freeze-drying and a brief description of a new technique whereby ampoules and small bottles may be freeze-dried without preliminary freezing in a separate chamber.

The author's interest in freeze-drying originated in 1935 and resulted in the development, through two pilot plants, of a large drying unit which produced over 300,000 transfusion bottles of dried plasma and serum in the 2½ years of its operation from February 1943. The author, and his colleagues of the MRC Drying Unit, are to be congratulated on a fine achievement. These plants are described in part III of the text and illustrated by many photographs and diagrams which contribute to make this an interesting report of an important wartime project.

GERIATRICS

1061 Medical Aspects of Growing Old

A. T. Todd. Bristol, John Wright & Sons Ltd., 1946. 164 pages; 13 figures. 22 x 14 cm. 15s. [£0.75]

(i) Introduction ; (ii) the problem of old age ; (iii) the mentality of the old ; (iv) digestive processes ; (v) digestive processes (cont.) ; (vi) digestive processes (cont.) ; (vii) on retirement ; (viii) exercise and exercises ; (ix) sleep ; (x) constipation ; (xi) the heart and circulatory system ; (xii) blood-pressure ; (xiii) emphysema ; (xiv) care of the nose ; (xv) care of the skin and hair ; (xvi) care of the feet ; (xvii) genito-urinary troubles in men ; (xviii) genito-urinary troubles in women ; (xix) conclusion. Appendices. Index.

Dr. Todd has written a small book, useful alike for the general practitioner and for the intelligent layman. He bases his thesis on the principle that the cultivation of health is more important than the treatment of disease; that whereas growing old is an inevitable process, yet many of the accepted signs of old age are really the manifestation of pathological changes which can either be prevented or rectified. Of the first importance Dr. Todd places a proper study of diet. He disclaims any validity for rigid uniformity in diet, and thereby honours the old adage that " one man's meat is another's poison ". While everyone may not agree with all of Dr. Todd's theories of diet, a large number will be readily accepted, while his remarks on milk and on cooking will claim wide appreciation. The reasons for and his definition of a " fat-free " diet for the elderly are convincing and simple of practice.

On the questions of sleeplessness and constipation, Dr. Todd's clear-headed thinking should go a long way towards resolving many a neurotic approach to these subjects, and should be read by all who are worried by the problems of " inner cleanliness "[1] with all its attendant horrors.

In an ageing population, Dr. Todd recognizes the need for keeping the elderly usefully and happily employed for as long as is possible. The theory of compulsory retirement at a given age has not only lost to the community a large number of persons whose work can ill be spared, but has led to a considerable amount of unhappiness and boredom among elderly people.

The description of simple exercises for the elderly, coupled with a number of simple hints on the attention necessary to the skin, hair and feet, completes a useful handbook for those interested in the care and management of old age. One hopes that this little work will be widely studied.

A.

[1] [A catchphrase used in advertisements for a proprietary saline purgative.—ED.]

HUMAN ECOLOGY IN THE MIDDLE EAST

1062 Middle East Science

A Survey of Subjects other than Agriculture. A Report to the Director General, Middle East Supply Centre, August, 1945

E. B. Worthington. London, His Majesty's Stationery Office, 1946. xiii + 239 pages; 16 plates; 5 maps. 25 x 16 cm. 7s. 6d. [£0.375]

Introduction. (i) Basic problems ; (ii) surveys and the land ; (iii) geology ; (iv) meteorology ; (v) rivers ; (vi) underground water ; (vii) domestic supply, water rights, and lessons from the past ; (viii) plants and animals ; (ix) forestry ; (x) marine fisheries ; (xi) inland fisheries ; (xii) human diseases ; (xiii) nutrition ; (xiv) health and medical services ; (xv) population and social studies ; (xvi) review. References to literature. Appendix I. Appendix II. Index.

Those who have had the privilege of reading Dr. Worthington's *Science in Africa* will expect a high standard in this his later work on *Middle East science*, and they will not be disappointed. Furthermore, though he deals specifically with the Middle East, much of what he has to say will find a far wider application and many who are living and working in other countries will gain no little interest and instruction from this volume which might aptly be entitled " Demography, with illustrations from countries of the Middle East ". It deals with climate, race, soil, nutrition, health and welfare; in short, the physical conditions and resources of these countries and " the interaction between man and his environment ".

The area covered is extensive and includes Persia, Saudi Arabia, Sheikdoms of the Persian Gulf, Aden, Ethiopia, Eritrea, Somaliland, the Sudan, Cyrenaica, Tripolitania, Palestine, Lebanon, Syria, Iraq, Cyprus and Malta. It would be impossible in a single volume to deal with each of these separately, so the author has, wisely, arranged his report so as to treat of subjects and not districts and to illustrate his points by examples selected from any part of this wide area.

The first chapter, " *Basic problems* ", forms an introduction to the author's method of approaching his great task. He shows how, in this area, are to be found all the stages of human development: first, hunters, as in the more remote parts of Ethiopia, Persia, Arabia and the Sudan; next, shepherds, as in the Arabian Peninsula, parts of Persia, Syria and the southern Sudan; thirdly, cultivators, in the valleys of the great rivers, the Euphrates and the Tigris, and in parts of Lebanon, Palestine and Transjordan; and, lastly, industrial workers, mostly in small rural industries and those engaged in the extraction of oil and minerals, and workers with wood and metal. He shows how, if progress is to take place, fundamental and technical knowledge must be translated into practice.

Dr. Worthington, by way of preliminary, demonstrates the environment and conditions of life of the inhabitants of the several countries, the geology, meteorology, climate and water-supplies, both superficial as from rivers and streams, and underground from wells and springs, and so passes on to irrigation and domestic storage. Next, the flora and fauna, the value, effects and uses of the forests among the former, and, among the latter, especially fisheries, fish-farming and culture, and by natural sequence to a consideration of the people themselves, their nutrition, their ailments and the modes of dealing with them and of the wider view of health services. A penultimate chapter, statistical in nature, tells of populations and population-trends and social studies, and the final chapter is of a review character, summing up aptly and succinctly all that has gone before. To construct and write an able epitome of so much detail must have been a difficult task and the author has succeeded admirably in putting the reader in possession of the main facts, enabling him to grasp the elements and the salient features of all the preceding chapters and thus, in the absence of a full index, directing him where he can find more detailed information on such subjects as most interest him, or on which he is seeking guidance.

None of this knowledge is superfluous if properly-adjusted and fruitful planning is to be achieved, and all ill-defined, haphazard planning is woeful waste; hence the importance of first trying out small-scale planning, of holding fast that which is good and then adopting these principles and adapting them for planning on a larger scale.

When we bear in mind that the area dealt with includes nearly a score of countries of widely differing characters—independent States, Sheikdoms, Crown Colonies, Protectorates, Mandated Territories, and a Condominium—it will become obvious why they could not be all dealt with fully within the compass of a single volume, and the wisdom of the author's scheme is revealed.

The chapters (XII–XIV) devoted to health and disease are models of epitomized information. Something is said on each of the principal diseases and the problems they involve, without overstepping the line separating general interest and importance from minutiae which are the concern of the specialist. The author stresses the dependence of *malaria*, the most widespread of all the diseases, on agriculture; development of agriculture diminishing its prevalence and severity in some parts, while in others irrigation and flooding may lead to multiplication of breeding-sites for mosquitoes and thus to increase of malaria. *Yellow fever* is endemic in parts of the Sudan and due note is made of the danger of its being introduced by aeroplanes and travellers in them into countries where the insect vector abounds and the inhabitants are susceptible non-immunes. The measures taken to control the spread of *sleeping sickness* (trypanosomiasis) in the southern Sudan and their success are duly mentioned. Reference will be found even to *onchocerciasis*, though it has but recently been reported in the Sudan. It is a disease common in West and Central Africa and in Mexico and parts of Central America. *Schistosomiasis*, one of the modern plagues of Egypt, is dealt with fairly fully, as its ill-effects warrant. *Ankylostomiasis*, or hookworm disease, is also rife, though less than the last-named. The mode of infestation of man was originally discovered by Looss in Egypt in 1897. *Typhus* and *relapsing fever*, louse- and tick-borne, and enteric diseases, *typhoid fever* and *dysentery*, conveyed by water, food and flies, all receive attention, as do the important eye diseases, especially *trachoma*, and *tuberculosis* which is rife, and *leprosy*, which is less common.

Nutrition, considering its importance as a factor both of health and of disease, is disposed of in a few (7) pages in which a general account is given and also references to recent studies and research. A good résumé follows of health and medical services, including hospitals, health-centres, dispensaries, laboratories and research-facilities in the different countries and the training of doctors—there are nine medical schools—and of dentists, of subordinate staff, pharmacists, nurses, midwives, and sanitary inspectors.

Much study and personal observation have been put into the writing of this book. In the bibliography there are 200 references to books, articles, papers and pamphlets, and there is a list of 235 persons whom the author consulted personally for information. The work is embellished by 16 photographs, well reproduced, and all of interest; one longs for more such. There are two maps showing the countries with which the Middle East Supply Centre was concerned, one showing the physical features, the other the vegetational distribution. In addition, there are three line-maps embodied in the text, omitting all confusing and unnecessary detail, to illustrate the river-systems, the irrigated land and the swamp-areas.

One criticism we think should be made, because the defect can be remedied in a future issue, and that is the unsatisfactoriness of the index. Almost without exception the reference consists of a single word. Selecting one at random, we find Humidity, with 6 page-references, all of which might have to be read to find the information sought. How much more helpful would it be to use sub-titles, such as: Humidity and air-conditioning, H. and climate, H., effects of, on health, on insect development, on mental and physical activity; H., measurement of; H., natural and water supplies; H., variability of in the Sudan, and so on, for all these points are mentioned in the text. Apart from this, the whole is excellent; misprints are very few, the print is clear and the binding adequate, and general format pleasing. The work deserves to be widely read.

H. Harold Scott

MEDICAL HISTORY AND PHILOSOHPY

[1036] Dynamische Reaktionspathologie

Die Uberwindung der medizinischen Grundlagenkrise durch die moderne Physik und Biologie

Entwicklung und Ziele einer eigengesetzlichen Medizin und ihre Auswirkung in Forschung, Praxis und Gesundheitspflege

K. v. Neergaard. Basel, Benno Schwabe & Co., 1946. 317 pages. 24 x 17 cm. Sw. fr. 24

(A) Problematik der heutigen Medizin; (B) Wandlung des naturwissenschaftlichen Fundamentes; (i) Grundbegriffe und Denkformen der klassischen Physik als Fundament der heutigen Medizin; (ii) Grundbegriffe und Denkformen der modernen Naturwissenschaft als Fundament der zukünftigen Medizin; (C) Entwicklung einer dynamischen Reaktionspathologie; (i) Die praktische Auswertung der klassischen und modernen Physik; (ii) Umbau der wissenschaftstheoretischen Struktur der Medizin unter dem Einfluss der modernen Physik und Biologie; (D) Organisatorische Auswirkungen; (i) Von der Individual- zur soziologischen Medizin; (ii) Hausarzt- Spezialarzt; (iii) Uberwindung der Nachteile des Spezialistentums; (iv) Unterricht; (v) Forschung; (vi) Organisation der Gesundheitspflege; Gesundheitspolitik, Gesundheitswirtschaft und ihre Beziehung zur Sozialversicherung. Schluss. Literatur.

[For review, see *BMB* 1036.]

[1044] Some Chapters in Cambridge Medical History

Sir Walter Langdon-Brown. Cambridge University Press, 1946, viii + 119 pages; 19 x 13 cm. 6s. [£0.3]

(i) John Caius and the revival of learning; (ii) William Gilbert and the dawn of experiment; (iii) Francis Glisson and the insurgent century; (iv) William Heberden and the age of reason; (v) John Haviland and the beginning of reform; (vi) the great triumvirate and the rise of the medical school; (vii) Clifford Allbutt and the transition from the nineteenth century. References.

[For review, see *BMB* 1044.]

[1045] The Life and Letters of Jonathan Hutchinson

Herbert Hutchinson. London, William Heinemann (Medical Books) Ltd., 1946. viii + 257 pages; 12 plates. 22 x 14 cm. 12s. 6d. [£0.625]

(i) Early family history; (ii) the apprenticeship; (iii) the first years in London; (iv) Jane Pynsent Hutchinson; (v) early married life (at Finsbury Circus); (vi) letters, 1866-71; (vii) the New Sydenham Society; (viii) the London hospitals and medical teaching; (ix) medical work 1859; (x) antiseptic surgery and anaesthetics; (xi) the medical societies; (xii) a holiday chapter, Germany and Denmark; (xiii) Cavendish Square; (xiv) Haslemere; (xv) letters, 1878; (xvi) letters, 1879-80; (xvii) letters, 1881-2; (xviii) letters, 1883-4; (xix) letters, 1885-7; (xx) educational work, Haslemere and Selby; (xxi) medical work, 1890-1900; (xxii) leprosy; (xxiii) a synopsis; (xxiv) the last years. Index.

[For review, see *BMB* 1045.]

[1049] New Aspects of John and William Hunter

Jane M. Oppenheimer. London, Wm. Heinemann (Medical Books), Ltd., 1946. xviii + 188 pages; 5 illustrations. 21 x 13 cm. £1 5s. [£1.25]

Part I: Everard Home and the destruction of the John Hunter manuscripts. (i) Introduction; (ii) Everard Home during Hunter's lifetime; (iii) Everard Home after Hunter's death; (iv) The holocaust; (v) Everard's defense. Notes for Part I. Bibliography. Appendix: Everard Home's publications. Part II: William Hunter and his contemporaries. (i) Introduction; (ii) William Hunter's entrance into the world of affairs; (iii) William Hunter and David Hume; (iv) William Hunter's political vacillations; (v) William's motives. Notes for Part II. Bibliography. Index.

[For review, see *BMB* 1049.]

MEDICAL MICROBIOLOGY

1063 The Cultivation of Viruses and Rickettsiae in the Chick Embryo

W. I. B. Beveridge & F. M. Burnet. London, His Majesty's Stationery Office, 1946. (Medical Research Council Special Report Series No. 256). viii + 92 pages; 10 illustrations. 24 x 15 cm. 2s. [£0.1]

(i) Introduction; (ii) techniques of inoculation and lesions produced; (iii) focal lesions on the chorioalantois; (iv) factors influencing susceptibility of the chick embryo to minimal amounts of virus; (v) the cultivation of individual viruses and rickettsiae; (vi) cultivation of bacteria, protozoa and foreign tissues in chick embryos; (vii) references.

In 1936 Dr. F. M. Burnet of Melbourne wrote one of the Medical Research Council's well-known "green reports" on *The use of the developing egg in virus research*. This described the technique, then quite a new one, of inoculation of viruses on to the chorio-allantoic membranes of developing chick-embryos. Eighteen viruses or related organisms had by then been studied in this way; the report ran to 58 pages with a page-and-a-half of references.

During the past decade the subject has grown enormously, and egg-inoculation has become the most important tool of current virus-research. Beveridge & Burnet's new report—though based upon the older one—covers a vastly wider field. It covers 92 pages (rather more closely spaced, now) with twelve-and-a-half pages of references; and the behaviour of 60 viruses in the egg is now described. The most important change is that infection of the chorio-allantoic membranes is now only one of many techniques which are available. True, it is still the most generally used. For primary isolation of some viruses, however, such as influenza and mumps, it is better to use inoculation into the amniotic sac. For growing rickettsiae and some viruses, inoculation into the yolk-sac is the method of choice. To obtain big yields of influenzal and related viruses for making vaccines, simple injection into the allantoic cavity is best. For other purposes the research worker may inject intravenously, into the extra-embryonic body-cavity, the albumen sac, or into the body of the embryo itself. There are various indications as to which of these methods is best for any purpose. Embryos of different ages are needed in different circumstances. Different temperatures of incubation may be required. To all these problems the authors offer a sure guide, and warnings are given as to the non-specific lesions which may lead the unwary astray.

The full account of the work carried out on 60 viruses is full of encouragement. Only 10 of these showed no signs of growing at all, 6 gave doubtful results, while 44 probably multiplied. (For a few of these 44, confirmatory evidence is still awaited.) This means that anyone tackling a "new" virus by techniques involving fertile eggs may entertain strong hopes that one or other will be of service to him. Even since the report went to press, a new triumph has been announced—the production by Shope and his colleagues of a vaccine against rinderpest, the virus having been suitably attenuated by growth in eggs.

C. H. Andrewes

1064 Virus as Organism

Evolutionary and Ecological Aspects of some Human Virus Diseases

Frank MacFarlane Burnet. Cambridge, Mass., Harvard University Press, 1946. 134 pages. 22 x 14 cm. 11s. 6d. [£0.575]

(i) Reproduction, variation, and survival; (ii) evolution and change in virus disease; (iii) the reaction of the host to virus infection; (iv) herpes simplex; (v) poliomyelitis; (vi) psittacosis and related infections; (vii) smallpox, alastrim, and vaccinia; (viii) yellow fever; (ix) influenza; (x) conclusion. Bibliography.

In this book, an expansion of his Dunham lectures given at Harvard in 1944, Dr. Burnet has developed part of the theme of his earlier work, *Biological aspects of infectious disease*, Cambridge, 1940. In that most stimulating volume, he treated his subject from the point of view of a biologist writing for biologists—including medical and other biological students. In *Virus as organism* he confines himself to virus diseases of man, and writes this time rather for medical men; but the theme is still the relation of parasite to host, and their inter-related evolutionary development. The history of infectious disease, so far as we know it, is of a surging tide of battle, of the waning of one plague and the waxing of another. Doctors, and especially those concerned with public health, will do well to read this book, to consider how the facts related apply to their own problems, and then to read it again, and perhaps again. The earlier chapters discuss in a general manner "reproduction, variation and survival", "evolution and change in virus disease" and "the reaction of the host". Then the author discusses his generalizations as they apply to herpes simplex, poliomyelitis, psittacosis, smallpox, yellow fever and influenza—diseases, the behaviour of which affords instructive contrasts.

The author suggests that in prehistoric man, living in quite small communities, there would be no opportunity for the occurrence of epidemic disease as we know it today. Only in the case of herpes will he allow that the man-virus association may be very ancient: for the other diseases he treats of, he looks for an origin within comparatively recent years—or at most centuries—from some virus-infection of other animal-species. In the case of poliomyelitis he refers to the related rodent-diseases, in psittacosis obviously to birds, in smallpox to domestic ungulates, in yellow fever to monkeys, in influenza, rather more hesitantly, to pigs. The thesis is a stimulating one, even though it may not always carry conviction. We should often do well to try, as he suggests, to understand infection by means of a "dynamic interpretation based on the changing requirements for survival of a virus whose environment is being altered by its host species' changing habits."

C. H. Andrewes

1065 A Text-Book of Bacteriology

R. W. Fairbrother. Fifth Edition. London, William Heinemann (Medical Books) Ltd., 1946. viii + 480 pages; 20 illustrations. 22 x 14 cm. 17s. 6d. [£0.875]

Part I: General bacteriology. (i) Historical survey; (ii) the morphology of bacteria; (iii) the biology of bacteria; (iv) the cultivation of bacteria; (v) the multiplication of bacteria; (vi) the destruction of bacteria; (vii) chemotherapy; (viii) infection; (ix) immunity; (x) antigens, antibodies and their reactions; (xi) hypersensitiveness: anaphylaxis, idiosyncrasy and allergy; (xii) the classification of bacteria; (xiii) bacteriology and medicine. Part II: Systematic bacteriology. (xiv) Staphylococcus, micrococcus and sarcina; (xiv) streptococcus; (xvi) pneumococcus: pneumonia; (xvii) neisseria: gonorrhoea: meningitis; (xviii) organisms of the coli-typhoid-dysentery group: genus bacterium; (xix) the Friedlander group and genus proteus; (xx) pasteurella: plague; (xxi) brucella: undulant fever: tularaemia; (xxii) haemophilus and associated organisms: whooping-cough; (xxiii) corynebacterium: diphtheria; (xxiv) mycobacterium: tuberculosis: leprosy; (xxv) vibrio: cholera: spirillum; (xxvi) pfeifferella: glanders: melioidosis; (xxvii) actinomyces: actinomycosis: madura disease; (xxviii) bacillus: anthrax; (xxix) clostridium: tetanus: gas gangrene: botulism; (xxx) miscellaneous genera: pseudomonas: lactobacillus: fusiformis; (xxxi) spirochaetes: syphilis: yaws: Weil's disease: seven-day fever: relapsing fever: Vincent's angina; (xxxii) filterable viruses; (xxxiii) the rickettsiae; (xxxiv) bacteriophage; (xxxv) bacteriology of water, milk and shell-fish. Part III: General technique. (xxxvi) The microscope: staining methods; (xxxvii) preparation of culture media; (xxxviii) serological technique. Index.

If reprints are included, this is the eleventh appearance of this book in less than ten years. No other tribute to its well-deserved popularity could be more eloquent than this fact. The medical student in Britain is expected to know enough of the technique of bacteriology to be able to perform simple examinations himself, but a great deal more about the theory of the subject, because this is fundamental to the understanding of infection as seen in the clinical field. He must know enough about diagnostic laboratory-tests to be able to interpret their results with a proper degree of reliance or scepticism, and perhaps rather more about immunology, because he should not only be proficient in common methods of artificial immunization, but capable of justifying their use to the sceptic. The book he needs must therefore be a nice blend of sound theory with not too much technique: the latter he should gain mainly from his practical classes. It should be readable and well-informed, and neither too long and detailed nor over-simplified. This is precisely the ideal which Fairbrother's textbook has attained. It is strictly a textbook of bacteriology—including, of course, filtrable viruses: the mistake is not made of including rather inadequate accounts of protozoa or helminths, and apart from an account of actinomycosis, mycology is omitted.

A highly significant innovation is the mention of the control of chemotherapy, along with diagnosis and specific therapy, as one of the main functions of bacteriology in medicine. The sulphonamides and antibiotics have indeed made the clinician more dependent on the laboratory and more alive to the services which it can render him. References to the chemotherapy of various infections are some of the new features in this edition: it evidently went to press too soon for anything to be said about the efficacy of streptomycin in both tularaemia and plague. Streptomycin is mentioned in connexion with tuberculosis, and it is also said that "The sulphonamides, in particular promanide, and penicillin have also given disappointing results". It is perhaps a little unfortunate to bracket these two treatments, because the sulphones have a very striking effect at least on experimental tuberculosis, whereas penicillin so obviously can have none that there are in fact no results at all, no one having ever deliberately studied so unpromising a form of treatment. The section on actinomycosis, although quoting Erikson's work showing that bovine and human strains of *Actinomyces* differ, still takes the view that the human disease is attributable to infection from an animal source. The more-commonly accepted present view is that the infection is autogenous. It is possible to offer only a few minor criticisms of this book, usually on matters of opinion rather than fact, and teachers may commend it to their students with confidence that it will nowhere lead them astray.

L. P. Garrod

MEDICAL POLITICS

1066 Now for Health

The What, Why and How of the National Health Service

D. Stark Murray & L. C. J. McNae. London, St. Botolph Publishing Co., Ltd., 1946. 78 pages. 22 x 14 cm. 4s. 6d. [£0.225]

(i) The past; (ii) the Health Bill; (iii) hospitals; (iv) the family doctor service; (v) the place of the local authority; (vi) the specialist and ancillary services; (vii) the opposition; (viii) the Health Centre; (ix) the citizen and the Health Centre; (x) democracy in the Health Service; (xi) education; (xii) farther yet. Appendix.

This booklet by Dr. D. Stark Murray and L. C. J. McNae expresses the opinions of the Labour Party on the future of the embryo which it has just conceived. The views are frankly prejudiced and indeed it would be strange if they were not, for Socialists have achieved as a result of hard work and much thought over many years the authority to carry into practice a plan which embodies with very minor exceptions all their doctrine. If, in their triumph, they are a little impatient of objections and tend to mention only a few of them purely in order to knock them down, that also is understandable.

The facts brought forward to support the case are well-marshalled and from unimpeachable sources. The unsatisfactory distribution of medical services of all kinds throughout the country, the heavy incidence of preventable disease in the lower economic group of the population, the very real difficulties of the mother and her children when sickness attacks them, the shortage of hospital beds and so on, are stated in such a way that no one could reasonably doubt their accuracy or importance.

Scattered throughout the text are a series of telling quotations from speeches of Labour members in support of the Bill in the House of Commons which indicate very clearly that the speakers were far from unaware of the problems of the proposed service. The authors, too, one of whom is a medical man, have a very sound knowledge of the doctors' difficulties, and their remarks on the profession are shrewdly calculated to suggest to the doctor that the new service is in his own interest, while so avoiding criticism as neither to antagonize him nor to make him lose face with a lay reader.

In outline the book is arranged in this manner. After a preliminary justification of the need for it, the Act is outlined. The important sections dealing with hospital services, general-practitioner service, the work of the local authorities and the health-centres are then justified separately, explained and the likely benefits described. A chapter on "The Opposition" dealing with the British Medical Association's views makes great play with the parallelism between the attitude of the British Medical Association to the introduction of national health insurance in 1911, and their present opposition.

This booklet, then, represents the case for the national health service of the present Government. As such it is a sound presentation, accurate and moderate in tone throughout.

A. C. Stevenson

MEN UNDER STRESS

1067 Men under Stress

Roy R. Grinker & John P. Spiegel. Second Edition. London, J. & A. Churchill Ltd., 1945. xii + 484 pages. 24 x 15 cm. £1 5s. [£1.25]

I. The men. (i) The men: their background and selection. II. The environment of combat. (ii) The combat units; (iii) motivation for combat-morale. III. The reactions to combat-morale. (iv) Reactions to combat, based on previous emotional disorders; (v) the neurotic reactions to severe combat stress; (vi) psychodynamics; (vii) treatment and results. IV. The reactions after combat. (viii) The return home; (ix) the syndrome of "operational fatigue" (war neuroses) in returnees; (x) passive-dependent states; (xi) psychosomatic states; (xii) guilt and depression; (xiii) aggressive and hostile reactions; (xiv) psychotic-like states; (xv) psycho-dynamics; (xvi) treatment: psychotherapy; (xvii) treatment: narcosynthesis; (xviii) treatment: adjunctive, and results. V. Civilian applications. (xix) Applications to civilian psychiatry; (xx) general social implications. References. Index.

The authors emphasize in their introduction that the neurotic reactions of aircrew, with which this book deals, are essentially the same as those of "Everyman in his struggle to master his own environment": consequently they believe that the lessons learnt from the cases they studied are applicable to the adaptations, and to the failures in adaptation, of normal citizens exposed to peacetime stresses.

A brief survey of the air-force personnel and a section on the structure, tensions and motives of combat units, lead up to a well-documented account of the immediate reactions to combat. The relation of these to previous emotional disorders is described, and then their recurrence in response to severe stress. A lucid and informative chapter on psycho-dynamics, and another on treatment, conclude this part of the book.

The next section, amounting to half the book, reviews in considerable detail the reactions after combat. The authors gained their experience of this while working in a convalescent hospital in the USA devoted to the rehabilitation of aircrew suffering from war-neuroses. They examine the "return home", the late manifestations of "operational fatigue", and the various states of dependence, guilt and depression, aggressiveness, and quasi-insanity which they noted in their patients. The psycho-dynamics of these conditions are elucidated, and the uses of psychotherapy, "narco-synthesis", and physical methods and hospital routine are expounded. The limitations of the authors' experience are illustrated by their statement that "we have not yet been able to test the efficiency of our treatment in enabling a flier to return to combat": but they seem, subject to this important qualification, to have been successful in restoring a high proportion of their patients to health and good occupational capacity.

The book is written in a clear, descriptive style. It relies greatly on psycho-analytical formulations, translated into untechnical language and making only the briefest overt reference to the libidinal aspect of the psycho-dynamics. It will be of considerable interest to those who have to deal with neurotic reactions to stress; but in its special application to air-force problems, it would perhaps have gained if the authors had paid regard to the published observations of the RAF and other neuro-psychiatrists, which covered a wider experience of combat-reactions than their own.

NEUROLOGY

1068 Introduction to Clinical Neurology

Gordon Holmes. Edinburgh, E. & S. Livingstone Ltd., 1946. vii + 183 pages; 37 figures. 24 x 15 cm. 12s. 6d. [£0.625]

(i) Symptoms and signs; (ii) pathology; (iii) examination of the patient; (iv) the motor systems; (v) muscle tone and co-ordination of movement; (vi) convulsions and other involuntary movements; (vii) examination of the motor system; (viii) sensation; (ix) examination of sensation; (x) reflexes; (xi) the visual system; (xii) movements of the eyes; (xiii) postural reactions and the vestibular system; (xiv) speech and its disorders; (xv) agnosia and apraxia; (xvi) the bladder and rectum; (xvii) the autonomic system; (xviii) mental state. Appendix. Index.

Everyone who has joined the throng which used to follow Dr. Gordon Holmes on his rounds at the National Hospital, Queen Square, London, will enjoy reading this book, and all, however erudite, will gain from it. Dr. Holmes has in this generation been the leading exponent of that form of clinical observation and argument which gave being to the english school of neurology, a school which led to a steady stream of senior students of neurology from every country to Queen Square.

Here is the application of physiological principle to clinical practice, and here is that emphasis upon the accurate observation of function which is so easily forgotten when laboratory methods are substituted for more-fundamental clinical ones. Here also is the elucidation of physiological principles by clinical observation, which will be remembered by so many who attended Dr. Gordon Holmes' ward-rounds and clinics. His personal teaching was so significant that there is no need to enlarge upon this aspect of his work. But the book is intended for students who are now approaching neurology, who have not this personal interest in it.

For them it is no more than its title, an introduction to clinical neurology, but it is an adequate introduction. It deals with fundamentals and the classification of disease has no place in it; in fact diseases are mentioned only incidentaly. The eighteen short chapters deal with different aspects of normal and abnormal functions of the nervous system. There are few illustrations, and the prose style is concise and rather hard, so that the student will have to take the reading seriously, but if he does so, his understanding of neurology will be increased. The text would be lightened by more diagrams, and it might be argued that it would gain by inclusion of descriptions of the diseases with which it is concerned. Dr. Holmes' aim was, however, to present only the basis of neurology in this introduction, and he has succeeded in a masterly way in this aim. All who have heard him teach will recommend the book to those who have not.

OPHTHALMOLOGY

1069 Lehrbuch der Augenheilkunde

Ernst Fuchs neu bearbeitet von *Adalbert Fuchs*. 18. Auflage. Wien, Franz Deuticke, 1945. xvi + 925 pages; 367 illustrations. 25 x 17 cm. Ost.S. 45

1. Teil: Einleitung. (i) Allgemeine Physiologie des Auges; (ii) allgemeine Pathologie. 2. Teil: Untersuchung des Auges. (i) Objektive Untersuchung des Auges; (ii) Funktionsprüfung. 3. Teil: Krankheiten des Auges. (i) Krankheiten der Bindehaut; (ii) Krankheiten der Hornhaut; (iii) Krankheiten der Sklera; (iv) Anatomie und Physiologie der Uvea, Entwicklungsgeschichte des Auges; (v) Krankheiten der Iris und des Ziliarkörpers; (vi) Krankheiten der Chorioidea; (vii) Glaukom; (viii) Krankheiten der Linse; (ix) Krankheiten des Glaskörpers; (x) Krankheiten der Netzhaut; (xi) Krankheiten des Sehnerven; (xii) Krankheiten der Lider; (xiii) Krankheiten der Tränenorgane; (xiv) Motilitätsstörungen des Auges; (xv) Krankheiten der Orbita. 4. Teil: Anomalien der Refraktion und Akkommodation. (i) Brillenlehre; (ii) optische Eigenschaften des normalen Auges; (iii) Myopie; (iv) Hypermetropie; (v) Astigmatismus; (vi) Anomalien der Akkommodation. 5. Teil: Operationslehre. (i) Allgemeine Bemerkungen; (ii) Operationen am Bulbus; (iii) Operationen an den Adnexen des Auges.

A reviewer cannot but be embarrassed in passing judgement on a textbook older than himself. Fuchs' *Lehrbuch der Augenheilkunde* first appeared in 1889, and the present volume is its eighteenth german edition. It has been translated into a number of foreign languages and an english edition helped greatly to mould a generation of ophthalmic surgeons who are only now passing from the scene.

The last three editions of the german text have been brought out by Professor Adalbert Fuchs, a son of the original author. The editor explains that the severe conjunctival and corneal lesions which so dominated ophthalmology at the end of the last century are not frequent now, but that he has hesitated to modify the text on these affections drastically, as his father had so greatly contributed to their elucidation, and his descriptions are used in various parts of the world as a guide to conditions still seen there. On the other hand he appears to have recognized that new problems and attitudes have emerged. The linking of ophthalmology with general medicine, the significance of genetic affections, the description of many syndromes, the emergence of new therapeutic agents, have all been taken into account.

Within the limit he imposed upon himself Adalbert Fuchs has done his task well. The book is still essentially the masterly text produced by his father, and, although note has been taken of new developments, the old framework rather obtrudes. It is this which makes the present volume essentially unsatisfactory. It would be both untrue and churlish to say that the text does not record the immense developments during the last twenty years, but it would be an act of excessive filial piety to hold that the text as a whole reflects them—and a classic is hardly a guide to current practice. It is, however, well to acknowledge that there is no other textbook of this size in opthalmology which contains such a mass of sound and systematized teaching. Ernst Fuchs was a great clinician, and some of his incidental remarks are revealing even today.

PATHOLOGY OF INJURY

1070 The Pathology of Traumatic Injury

A General Review

James V. Wilson. Edinburgh, E. & S. Livingstone Ltd., 1946. ix + 192 pages; 61 figures. 25 x 17 cm. £1

Part I. (i) Traumatic shock; (ii) the pathology of burns; (iii) crush injury —traumatic anuria; (iv) fat embolism; (v) blast injury; (vi) the pathology of wounds and wound infection. Part II. (vii) Injuries to the chest; (viii) injuries to blood vessels; (ix) abdominal injuries; (x) injuries to the nervous system; (xi) injuries to bones and joints. Index.

A great deal of work, clinical, pathological and experimental, has accumulated in the past few years on the nature and mechanism of traumatic lesions. Just as it took the stimulus of the 1914-18 war to popularize transfusion, so we may hope that civilian practice will benefit from the lessons learnt in this war.

It takes a good deal of effort, however, to digest even what has already been published, and to assess the very numerous studies, some valuable and others quite worthless, at their proper value. It is impossible to do this without a background of personal involvement in the problems. The author of this work rightly draws from his own experience as a pathologist with the RAMC in the Middle East and on this basis reviews the most important of the advances made. He has made no attempt "to write a complete text-book covering all aspects of the picture" and, since the book was written abroad, the references are necessarily incomplete. Even so, each chapter has a reference list of between 30 and 100 papers. There are 61 illustrations, many original and some in colour. The main patterns of traumatic lesions are first described; shock, burns, blast, crush-injury, wounds and wound infection and their lesions are discussed on a regional basis, dealing with the special problems raised by the blood-vessels, nervous system, bones, chest and abdomen.

An advantage of wartime pathology is evident, comparing this book with others written by civilian pathologists on the same subject, in that the author was in close contact with clinicians; the book is not a forensic study but promises to be of value to practising surgeons, since one is not allowed to forget that traumatic pathology is not only knowledge about a corpse of use chiefly to coroners, but concerns living patients, the subject of important decisions by the clinician.

If criticism can be made, it is firstly that armchair theorists and purely experimental pathologists receive too large a mention (e.g. in the chapter on shock) and secondly that the author prefers to leave open questions that could perhaps be summarized more succinctly. This is, however, erring on the right side; a personal bias only too easily imposes a uniform perspective on near events which turn out later to be many differing facets of wider and deeper views.

E. G. L. Bywaters

PENICILLIN PRIMERS

1071 Penicillin: Its Properties, Uses and Preparations

Council of the Pharmaceutical Society of Great Britain. London, The Pharmaceutical Press, 1946. viii + 199 pages; illustrations. 22 x 14 cm. 10s. 6d. [£0.525]

Preface. (i) Historical summary; (ii) commercial manufacture; (iii) chemistry and chemical properties; (iv) stability; (v) standard, unit and methods of assay; (vi) pharmacology; (vii) clinical use; (viii) pharmacy and pharmaceutical preparations; (ix) legal considerations. Appendices. Bibliography. Index.

This book has been published under the direction of the Council of the Pharmaceutical Society of Great Britain and provides a concise summary of the available information on the chemistry, pharmacy and clinical uses of penicillin. The information is reliable, well presented and judiciously selected and the anonymous author or authors are to be congratulated on the production of what is undoubtedly the best handbook yet published on this subject.

Now that penicillin has passed the stage of being boosted as "The Wonder Drug" and is taking its proper place among materia medica, it seems that it is likely to maintain its position as the most valuable therapeutic discovery of recent years. The early hopes of the discovery of a series of such antibiotics potent against different types of organisms have not been fulfilled, and except for the still-unproved streptomycin, it now seems unlikely that a rival to penicillin will be found in the field of natural antibiotics. This emphasizes Sir Howard Florey's description of penicillin as "quite one of the luckiest accidents which have occurred in medicine", though this should not in any way detract from the credit due to Fleming, since it seems highly probable that many bacteriologists before Fleming must have seen what he saw on his now-famous Petri dish, without appreciating its significance.

The chapter on commercial manufacture hardly emphasizes sufficiently the magnitude of the technical achievement of the large-scale production of penicillin. The technical difficulties which had to be overcome in adapting a biological process of this kind to a commercial scale are probably known only to those who actually took part in the work. That success was achieved was largely due to a chance observation by Moyer that the addition of corn-steep liquor to the medium gave a greatly increased production of penicillin. This discovery and the selection of high-penicillin-producing strains of mould have made the chief contribution to the increase in titre from the original one unit per ml. obtained by Florey to 200 or more units in modern plant.

The chapters of most value to the clinician are those on Stability, Pharmacology and Clinical Use, which give a clear description of the methods of administration and the precautions to be observed in practice. The destructive effect of certain types of

rubber tubing on penicillin is mentioned, but it is difficult to see what the user can do about it if he is not in a position to have tests of potency performed. Many of the suggestions which have been published for the prolongation of the action of penicillin are described, but it seems that the only method which has found general acceptance is the suspension in beeswax and arachis oil or the modification containing ethyl oleate. The use of hydrogenated cottonseed-oil which has been found satisfactory in the USA is not mentioned. There seems to be a trend towards the use of still higher doses than mentioned here.

A book on a new subject such as this is bound soon to become out-of-date in many respects, and it is to be hoped that the Pharmaceutical Society will issue a new edition before this can happen.

The book is well illustrated with many diagrams and photographs and contains a comprehensive bibliography. No misprint or error has been detected by the reviewer. It can be confidently recommended to anyone who wishes to become familiar with the penicillin story, and should be especially useful to the general practitioner.

Norman Evers

1072 La Pénicilline à la Portée du Praticien et son emploi dans le traitement des maladies vénériennes

Jean Monnier. Paris, Librairie J.-B. Baillière et fils, 1946. 148 pages; 26 figures. 24 x 16 cm.

(i) Historique ; (ii) production de la pénicilline ; (iii) propriétés biologiques de la pénicilline ; (iv) comment soigner par la pénicilline ; (v) traitement des maladies vénériennes ; (vi) traitement des maladies vénériennes (suite). Bibliographie.

This book, by a medical officer to the french naval forces in Britain, opens with a preface by Sir Alexander Fleming, in which he sketches the chain of events in his discovery of penicillin and in its further development by the Oxford team.

The author makes no claim to have produced a " contribution to the study of penicillin ". He has simply tried to group together, in a practical order, information which will help the practitioner in France, who has been out of touch with foreign work during the german occupation, to make good use of penicillin when it becomes generally available in that country.

The book falls into two parts, the first four chapters dealing with penicillin from a general point of view, while the last two are devoted to its use in the treatment of venereal diseases. A brief historical sketch of the discovery and development of penicillin, with a note on other antimicrobial substances evolved by fungi and microbes, is followed by a chapter on the production of penicillin and another on its biological properties. The general part of the book ends with a long chapter on the clinical use of penicillin methods of administration, dosage, reactions, bacteriological methods in connexion with treatment and control methods.

Of the two chapters on treatment of venereal disease, which occupy nearly half the book, one is devoted to syphilis and the other to gonococcal infections.

The book is well illustrated with graphs, drawings and photomicrographs, and is well provided with tables. There is a general bibliography of over 150 references and a shorter separate list of references to treatment of venereal diseases by penicillin.

A. H.-S.

PHYSIOLOGY AND PHARMACOLOGY

1073 Estado Actual de la Farmacología Arsenical

A. Esteve & A. Oriol. Madrid, Barcelona, Editorial " Miguel Servet ", 1946. 139 pages; 39 figures. 20 x 14 cm.

(i) Química de los arsenicales ; (ii) de la química a la farmacología ; (iii) discusión de la crisis nitritoide ; (iv) otro aspecto de la toxicidad arsenical ; (v) indices quimioterápicos y el problema de las negativizaciones serológicas ; (vi) metabolismo arsenical ; (vii) acción idiotópica de los arsenicales ; (viii) acción idiotópica de los arsenicales (cont.). Bibliografía.

In this monograph the authors review the pharmacology of some organic arsenical drugs used in therapeutics. After referring to Ehrlich's original researches and to Voegtlin's conception of the conversion of arsphenamine to arsenoxide in the body, they proceed to describe some of the physico-chemical properties of neo-arsphenamine. Numerous titration-curves show the buffer action of solutions of this drug and the authors point out that the isoelectric points of normal blood and of neo-arsphenamine are the same (isoelectric point pH 7.36). Theoretically, a small change of blood pH could produce a large change in the degree of dissociation of the drug and this, the authors suggest, might account for abnormal reactions which sometimes occur after the drug is injected.

On the problem of nitritoid reactions studied experimentally in the dog, they state that the fall of blood-pressure after intravenous injection of arsphenamine occurs only in the unanaesthetized animal. Thus, anaesthesia with chloralose abolishes the effect but morphine alone does not. The authors believe that the nitritoid reaction is associated with changes in some of the physical properties of the blood such as in the surface-tension, the viscosity and in the electric charge on the globulins. There follows next a discussion of the chemical toxicity and therapeutic activity of arsenobenzenes in which the authors argue that the tests for therapeutic potency need to be applied more rigorously.

Injected arsenobenzenes, such as arsphenamine, are known to be rapidly absorbed by the tissues. The highest concentration of arsenic is found in the liver and spleen, and histological evidence suggests that it is fixed mainly in the reticuloendothelial cells. Much still remains to be discovered about the excretory products of arsenobenzenes in the urine. The last and eighth chapter deals with the affinity of the sulphydryl group for arsenic and with the value of various antidotes; but it is apparent that information on BAL (2 : 3-dimercaptopropanol) had not reached the authors in time for inclusion in this monograph.

This monograph contains 72 references and, presumably, is intended for the general reader. Even so, the authors pass hurriedly from one subject to another and give the impression of superficial treatment of the data which they have selected for discussion. There are numerous misspelt words in the list of references.

H. M. Adam

1074 Histamina e Anafilaxia em suas relações com a Patogenia das doenças alérgicas

M. Rocha e Silva. São Paulo, Gráfica e Editora Edigraf Ltda., 1946. 331 pages; 56 figures. 23 x 16 cm. Cr. 90,000

(i) Propriedades farmacológicas da histamina ; (ii) choque anafilático e fenômenos alérgicos ; (iii) mecanismo do choque anafilático ; (iv) choques produzidos pela peptona, tripsina e venenos animais ; (v) histamina ligada e histamina livre ; (vi) efeitos da histamina sobre a pele : papel da histamina na inflamação aguda ; (vii) idiossincrasia a drogas e medicamentos ; (viii) o problema geral da alergia humana ; (ix) substâncias anti-histamínicas e terapêutica das doenças alérgicas ; (x) resumo histórico e conclusão. Bibliografia geral. Índice analítico.

In this monograph the author first sets out what is known of the physiological changes that occur in experimental anaphylaxis and allergy, and then discusses how far the experimental facts explain similar phenomena in man.

In 1920, Dale advanced the theory that anaphylaxis was due to the liberation in the tissues of histamine and possibly other pharmacologically-active substances. In tracing the development of experimental work based upon this conception, the author summarizes in the first chapter the pharmacology of histamine and, in the second chapter, the features of anaphylactic shock and other types of tissue reaction. He then goes on to discuss in chapter III the mechanism of anaphylactic shock and the evidence for preformed histamine and its release in the body. This leads him to a description in chapter IV of analagous forms of shock induced by peptone, trypsin and various animal-poisons. This chapter and the next are, perhaps, the most interesting since they embody much of the author's own work on the release of histamine.

Earlier work on the action of trypsin was limited by the impurity of the material. Rocha e Silva was the first to study the pharmacological properties of crystalline trypsin. He showed that trypsin acted in many ways like histamine, that it released histamine in the tissues, and that its effects were similar in many respects to those of anaphylactic shock. These facts suggested that histamine was bound by a peptide linkage to amino-acids, and Bergmann's work on synthetic substrates for trypsin indicated that these might be arginine and lysine. While working in Bergman's laboratory, Rocha e Silva made a number of chemical models of bound histamine by joining histamine to various amino-acid derivatives. These compounds were all pharmacologically inactive, but became active after hydrolysis, that is, after the liberation of free histamine.

After considering the evidence, the author arrives at the following hypothesis to account for the phenomena of anaphylaxis. Histamine is reversibly bound to amino-acids, probably arginine and lysine, by a peptide linkage. This linkage can be broken directly, by injected proteolytic enzymes, animal poisons or by thermal injury ; or, it can be broken indirectly, by antigen and peptone. Now, in the sensitized body, antigen in some way unknown disrupts the blood-platelets and so liberates a platelet kinase which in turn activates plasma trypsin and possibly intracellular protease. These enzymes then attack peptide linkages and liberate free histamine and possibly other substances, which act on cells at or near the site of liberation. We may, indeed, quote the author's words: "the problem today is to know which trypsin or which proteolytic enzyme could really be the precipitating factor".

In Chapter V is included also a discussion of Ackermann's work on the pharmacodynamic groups of the histamine molecule. Chapter VI is on the effects of histamine on the skin and the role of histamine in acute inflammation. Menkin's work on leukotaxine is criticized on the ground that the effect of leukotaxine on the permeability of skin-capillaries could be due to histamine liberated in the skin. The chemotactic property of leukotaxine is not discussed. In the remaining four chapters, drug idiosyncrasy, allergic diseases and antihistamine drugs are dealt with in turn. The classification of the hypersensitive states is based on physiological considerations and is, therefore, logical and simple. The author purposely avoids cumbersome terminology. The chapter on antihistamine drugs will, no doubt, be expanded in future editions. Neoantergan, a potent synthetic antihistamine, which was reported in the literature in 1944, is not mentioned; but this omission may have been caused by wartime difficulties in the exchange of literature.

The monograph is well printed and contains a list of 700 references and 69 illustrations, 4 of which are in colour. The author is to be congratulated for having made a valuable contribution to the literature on histamine and to a large and important part of medicine, for in this monograph are fundamental notions on disease of interest to the physician, surgeon, dermatologist and pharmacologist alike. It is to be hoped that the translation of this work from portuguese into english will not be long delayed.

H. M. Adam

RADIOGRAPHY

1075 A Descriptive Atlas of Radiographs

An Aid to Modern Clinical Methods

A. P. Bertwistle. Sixth Edition. London, Henry Kimpton, 1946. xxix + 606 pages; 948 illustrations. 25 x 18 cm. £2 5s. [£2.25]

Milestones in radio-diagnosis. (i) Normal bones and epiphyses ; (ii) congenital abnormalities ; (iii) fractures ; (iv) diseases of bones ; (v) tumours of bone ; (vi) injuries and diseases of joints ; (vii) nasal system ; (viii) dental system ; (ix) alimentary system ; (x) urinary system ; (xi) respiratory system ; (xii) nervous system ; (xiii) vascular system ; (xiv) ductless glands ; (xv) female generative system ; (xvi) muscles ; (xvii) medico-legal ; (xviii) anthropology ; (xix) helminthology. Index.

The author has continued to assemble from many sources radiographs illustrating various pathological lesions, for the most part advanced. Many of the illustrations are first-class. Accompanying each is an altogether too brief account of the clinical history and description of the radiographic appearances. Apart from an increase in the number of plates with their legends, this edition continues to have the book's former defects, for it is based on wrong premises, i.e. that radiology can be learnt by the study of an atlas. Radiology cannot be learnt by the novice from an atlas, however good and comprehensive its illustrations and however full its descriptions, no more than pathology can be learnt from museum specimens.

The radiographic manifestations of disease are infinite, so that an atlas ten times this size, compiled by an expert, would still leave much to be desired by the competent radiologist. Yet the medical man who has not had the training, which is now available at most medical schools, must find the resemblances very confusing, even in the moderate number of illustrations of this volume—a confusion which is not unravelled by the inadequate and in some cases erroneous descriptions—for example, the legend of fig. 399 (p. 278). Because this method of learning radiology has been followed in the past, illustrated descriptions of many lesions have appeared in the literature under wrong titles, solely because the authors thought that the radiographic appearances resembled those in cases previously described. Such erroneous descriptions and plates have been copied or used in other articles and caused widespread confusion.

As the author indicates in his introduction, early diagnosis is most desirable. Unfortunately the indications of early disease are apparently insignificant, and difficult or impossible to reproduce. Printed by the ordinary methods, an atlas such as this cannot show them. It is difficult even for the radiologist to detect the lesion of old-established disease described, as illustrated in the frontispiece of this book.

James F. Brailsford

1076 A Handbook of Radiography

John A. Ross. Second Edition. London, H. K. Lewis & Co. Ltd., 1946. viii + 164 pages; 79 figures. 22 x 14 cm. 10s. 6d. [£0.525]

Preface. (i) Care of the patient ; (ii) taking a film ; (iii) the dark room ; (iv) the extremities ; (v) skull and sinuses ; (vi) teeth, jaw and face ; (vii) the spinal column, etc. ; (viii) the thoracic viscera ; (ix) the alimentary tract ; (x) other abdominal viscera, renal and female genital tracts ; (xi) the localisation of foreign bodies ; (xii) soft tissues ; (xiii) radiography of depth and movement ; (xiv) neuro-radiology ; (xv) elementary *x*-ray physics. Appendix. Index.

The author of this small book is to be congratulated on writing a very readable volume which no radiographer could read without deriving some benefit; many would profit considerably from the lessons on the treatment and care of the patient, the taking of the film, its processing in the darkroom and the making of copies. The technique to be observed in taking radiographs of all the bones and joints is so clearly explained and illustrated that the radiographer will have no difficulty in preparing the radiographs essential for the radiologist to give good interpretation. The same can be said of the radiography of the chest, the alimentary tract, the diaphragm and liver, gall-bladder, genito-urinary tract. Various methods for the localization of foreign bodies are described. The special features of stereoscopy, tomography and neuro-radiography are clearly and concisely described and illustrated. The book concludes with a chapter on elementary *x*-ray physics.

James F. Brailsford

1077 Field Service Handbook of Practical Radiography

The War Office. London, His Majesty's Stationery Office, 1945. iv + 141 pages; 146 figures. 18 x 12 cm. 2s. 6d. [£0.125]

Introduction. (i) General preliminaries to *x*-ray examinations ; (ii) the upper extremity ; (iii) the lower extremity ; (iv) the spine ; (v) the thorax ; (vi) the skull ; (vii) the jaws and teeth ; (viii) the thoracic viscera ; (ix) the abdominal viscera ; (x) stereography and localization ; (xi) marking, filing, disposal of radiographs and quarterly reports ; (xii) administration of radiological departments ; (xiii) photographic aspects of radiography ; (xiv) packing of *x*-ray truck with M.X. 2 equipment. Index. Appendices. Tables.

This small pocket-book was drawn up for the use of men in the armed forces whose duty it was to conduct *x*-ray examinations in advanced stations. The introduction contains the following healthy comment:—"In forward areas when considering radiology, the fundamental question should be: 'Is an *x*-ray examination really necessary at this juncture?'" To those who can answer in the affirmative the book is a concise, well-arranged and instructive manual. The essential positions required for demonstrating all parts of the skeleton and for conducting all the routine radiographic examinations of the systems are clearly stated and illustrated. Its very modest price, size and sound instruction are recommended to all radiographers. It can be favourably compared with more expensive volumes which set out to achieve the same object.

James F. Brailsford

1078 A Manual of Tomography

M. Weinbren. London, H. K. Lewis & Co. Ltd., 1946. viii + 270 pages; 397 illustrations. 25 x 19 cm. £2 5s. [£2.25]

(i) Introduction ; (ii) tomography of the chest ; (iii) tomography of the spine ; (iv) tomography of the skull and facial bones ; (v) miscellaneous ; (vi) tomography of the larynx ; (vii) technique. References. Index.

In this volume the author explains the physical factors which permit us to obtain a section-radiograph of the body in its long axis at any depth. At the selected level the main outlines of the structures are seen because these are fixed while the structures in front or behind are blurred by movement. The author describes the technique which he has enthusiastically applied to the examination of lesions of the chest, spine, bones and joints, skull including facial bones, larynx and various parts of the alimentary canal, gall-bladder and urinary tract. His findings in these many spheres are illustrated with plain radiographs for comparison. A study of these brings one to the conclusion that in only a few cases does the tomograph render what may appear to be additional evidence—in the majority of cases the plain radiographs, particularly when interpreted in the light of other radiographs taken in other planes, i.e. antero-posterior with lateral or oblique, give accurate evidence without permitting the licence in interpretation which may be indulged in with the tomograph. The method is expensive in material and time, particularly in a department busy with routine work. It is very doubtful if there is any evidence of a lesion illustrated by tomography in this book which could not have been at least equally obtained by radiography in one or more planes, or by stereoscopy.

James F. Brailsford

SERVICES FOR PHYSICAL AND MENTAL HEALTH

1079 Neurosis and the Mental Health Services

C. P. Blacker. London, Humphrey Milford, Oxford University Press, 1946. xxii + 218 pages. 22 x 14 cm. £1 1s. [£1.05]

Introduction. (i) Origins, history and scope of the survey. Part I: The survey: main findings and their interpretation. (ii) Preliminary notes: circumstances affecting the survey: presentation of findings; (iii) main findings summarized; (iv) questions arising from the findings; (v) neurosis in industry. Part II: Post-war psychiatric services: long-term considerations. (vi) Introduction; (vii) training of psychiatrists: the teaching psychiatric unit; (viii) training and registration of mental nurses; (ix) children's services; (x) the role of the mental hospital in a mental health service; (xi) proposed mental health services for a population of a million; (xii) the medical officer of mental health; (xiii) accessory services; (xiv) the prevention of mental infirmities: the social problem group; (xv) miscellaneous. Part III: Post-war psychiatric services: short-term considerations. (xvi) The post-war transitional period. Part IV: Main findings of the survey. (xvii) Description of findings. Appendices. Index.

Dr. Blacker was entrusted in 1942 with the task of surveying the psychiatric out-patient services of England and Wales. Before long it became evident that the findings would be relevant to the larger problem of how the mental-health services should be developed to meet the requirements of a national health scheme. Consequently the report falls into two parts: the first gives a very detailed analysis of the existing provision which amounted to 216 out-patient clinics very unevenly distributed, and the second embodies recommendations for the growth and better organization of all the mental-health services.

The inequalities in distribution of out-patient facilities were remarkable. Whereas, for example, in Kent and Sussex there were 9.14 clinics per million of population, in the Lancashire and Cheshire region the proportion was 3.66 per million. The number of doctor-sessions per week similarly varied in different regions and for different types of clinic: 4.96 in London, but only 2.05 in the county boroughs outside London, and 1.42 in administrative counties. Measured in relation to the population served, it ranged from 26.7 per million in the London region to 4.94 for Wales. Like disparities were found when the accessory services (such as psychiatric social work), the pressure on clinical facilities, and the number of new patients and patients under treatment in the clinics of different regions were compared. Moreover, the clinics based on mental hospitals had apparently worked under great handicaps, being less well-equipped, holding fewer sessions and seeing proportionately fewer patients than the voluntary or independent clinics.

Dr. Blacker's recommendations are far-reaching. He reviews the needs broadly, and then sets out his detailed proposals for providing an area of a population of a million with comprehensive mental-health services. In the main, he advocates that for such an area a hundred beds should be provided in the first instance elsewhere than in mental hospitals, to accommodate patients who are not acutely ill and for whom certification as insane is not in question: additional beds would be required according to local arrangements for the acute or emergency cases now admitted into observation wards. The existing out-patient arrangements should be increased by 75 % to 100 %: child-guidance centres should be established on the minimum basis of one for every 20,000 children: three, or four, child psychiatric clinics should be established in the central psychiatric clinics of the region: there should be a hostel for unstable children, a reception-centre for sorting homeless children who have to be cared for otherwise than by their parents, and improved provision for mental defectives through colonies and community-care; more-adequate professional staffing of mental hospitals is also needed.

It is impossible in a summary to reproduce the cogent evidence and arguments on which these proposals rest. The book, which grew out of a wartime problem, represents a broadly conceived, practical and coherent scheme for providing a model postwar mental-health service. Some of its recommendations are already in process of being put into effect.

1080 Tuberculosis in the West Indies

W. Santon Gilmour. London, National Association for the Prevention of Tuberculosis, [1946]. 221 pages; 13 illustrations. 22 x 14 cm. 7s. 6d. [£0.375]

Foreword. Description of colony; population numbers and racial description; conditions of living; tuberculosis and vital statistics; existing facilities for diagnosis and treatment; tuberculosis survey; recommendations. Appendices. Barbados; Windward Islands; Grenada; St. Lucia; Leeward Islands; Antigua; St. Kitts; Nevis; British Guiana; Bahamas. Summary. Appendix.

This report is based on a visit in 1943-44 to Trinidad and other west-indian colonies (excluding Jamaica), under the auspices of the Colonial Office and the National Association for the Prevention of Tuberculosis. Two-thirds of Trinidad's population of half a million are of african, and one-third of east indian, origin, the former predominating in the towns and the latter in the rural areas. Apparently, housing conditions are still bad for the majority both in town and country; diet is deficient in proteins, vitamins and minerals; parasitic infestation is common; real earnings are low.

The recorded tuberculosis-mortality is 100 per 100,000, which is about 50 % higher than in Britain and double the United States figure; the urban rate is four times the rural. No reliable estimate of total cases in the island is given, but preliminary mass-radiography results indicate an incidence of 6·7 active cases needing treatment per 1,000 of the general public examined. Persons with tuberculosis fall mainly under the care of the Government's general medical services supported by a few clinics run by voluntary agencies and staffed by part-time workers; there is no whole-time tuberculosis officer, no sanatorium or special hospital. A tuberculin survey by the author showed 44 % positive to 0·01 or 0·1 mg. in urban schools and 22 % in rural schools; in the latter, african showed higher rates than did east indian children. The urban-rural contrast is attributed more to the overcrowding of dwellings in the towns than to racial factors. Bovine infection is rare in Trinidad and pulmonary disease is the rule. All stages of the adult type are found, but most are acute, and the average expectation of life after diagnosis is about 2 years; nevertheless, the population cannot now be considered as virgin soil, and successful treatment should be possible in many cases if diagnosed earlier than at present.

Among the author's recommendations, improved housing is given first place, and this should be combined with material inducements for a movement from town back to the land, and with health-education. A scheme for diagnostic clinics and tuberculosis hospitals, with experienced full-time medical, nursing, social welfare and other staff, is put forward; and the first sanatorium, already being built, will assist in this scheme. A scheme of maintenance-allowances for the tuberculous, somewhat on the lines of the british scheme introduced during the war, is suggested; also the value of rehabilitation is stressed. It is proposed that the Government shall be responsible for the services, and for any schemes of maintenance, rehabilitation and re-employment, leaving some of the aspects of social welfare and health-education to the voluntary agencies. In addition to his account of Trinidad, the author records shorter surveys of the tuberculosis position in Barbados, the Windward and Leeward Islands, British Guiana and Bahamas; the last-named colony has the highest tuberculosis death-rate of the West Indies.

1081 The Re-adjustment in Civil Life of Soldiers Discharged from the Army on Account of Neurosis

Eric Guttman & Elsie Thomas. London, His Majesty's Stationery Office, 1946. (Ministry of Health. Reports on Public Health and Medical Subjects, No. 93.) 72 pages; 4 diagrams. 24 x 15 cm. 1s. 3d. [£0.0625]

Introduction. The method; army service; present condition; regional differences; causative factors; diagnosis and outcome; treatment and outcome; pension; occupational resettlement; supplementary postal inquiry; further comments and discussion. Summary. Diagrams. Appendices. Tables.

This record of a systematic ".follow-up" inquiry has double value, since it not only indicates what social and medical consequences flow from neurotic disability in soldiers, but also demonstrates the method necessary for undertaking a thorough survey of the kind. The sample, consisting of 382 men, was drawn from a variety of rural and industrial areas: each man was visited, nearly always in his own home, by a psychiatric social worker who by persistent effort achieved the result, very rare for this type of field-work, that she succeeded in tracing and investigating every case; and the data were collated with those supplied by the Ministry of Pensions regarding the men's previous health-record. A check on the need for thorough ascertainment by a trained visitor was provided by a concurrent postal inquiry which, though of course much simpler and cheaper, yielded ambiguous and incomplete information.

Three-quarters of the men had required medical attention during the fifteen months after their discharge from the Army. Nearly all the men had to stay away from work because of their ill-health; the absence-rate was over 9 % of the possible working-time. 13 % had changed their job four or more times during the fifteen months: 6 % were unemployed at the time of the inquiry. A tenth of the men experienced serious domestic and social maladjustment, 9 of the men had been sentenced to prison since discharge, but 5 of these had had criminal records before they entered the army. Men who applied for pensions complained more of reduced working-capacity than the rest, but did not in fact differ from the total in respect of sickness-absence or frequency of change of employment.

The report as a whole gives a far-from-reassuring picture of the condition of neurotic soldiers after their return to civil life. But the group was not a normal one before enlistment: it had been characterized by earlier symptoms or breakdown and by poor adjustment to work. The authors of the report stress the need for increased psychiatric facilities for these men but hold that "their problems do not differ in principle from those of other neurotics, and it would not seem advisable to stress unduly the fact that their difficulties are connected with their army service". [Since this report was concluded, further efforts have been made, especially by the Ministry of Labour and the Ministry of Health, to improve the facilities for the industrial resettlement of the neurotically disabled.]

1082 National Health Insurance in Great Britain, 1911–1946

R. W. Harris. London, George Allen & Unwin Ltd., 1946. 224 pages. 22 x 14 cm. 12s. 6d. [£0.625]

Part 1. National insurance. Foreword. Introduction. (i) The scheme described; (ii) foundations; (iii) foundations; (iv) (*a*) types of societies administering the scheme; (*b*) effects on membership and funds; (v) administration; (vi) finance; (vii) the control of sickness benefit claims; (viii) insurance and national providence. Part 2. National health. Introductory note. (ix) The insurance medical service described; (x) foundations; (xi) the practitioners' remuneration; (xii) the machinery; (xiii) a short note on maternity benefit; (xiv) the insurance medical service; (xv) progress towards an organised medical service for the nation; (xvi) a complete national health service. Appendices.

The author of this book has been officially concerned with british national health-insurance for over thirty-five years. He was one of the civil servants engaged in revising the health provisions of the National Insurance Bill, 1911, and in helping Mr. Lloyd George to convert the Bill into an Act of Parliament. As an assistant secretary in the Ministry of Health he was largely responsible for the central administration of the health-insurance scheme; and since his retirement from the civil service he has been chairman of the medical service sub-committee of the London Insurance Committee. The book is the outcome of a study of national health-insurance undertaken in 1937 at the request of the Institute of Public Administration, and brought up to September, 1945. It is divided into two parts. The first deals with the administrative, financial, and provident aspects of health-insurance, the second with the insurance medical service created by the National Insurance Act, 1911.

In the first part, Mr. Harris shows that although, when in 1911 we adopted compulsory health-insurance on a national scale, we followed the example set by Bismarck in Germany in 1883—an example that had already been followed by some other continental countries—we did not make a leap in the dark. We had had in Britain several centuries' experience of health-insurance on a voluntary basis for our guidance: voluntary health-insurance in a rudimentary form was provided by the social guilds of the middle ages, and in a more fully developed form by the "friendly societies", whose history can be traced back to the sixteenth century, and whose work was commended in the seventeenth century by Daniel Defoe. Mr. Harris gives an interesting account of the rise and development of the "friendly society" movement, and shows the difficulties encountered by the early workers in the movement. One of the most serious was the lack of a sound actuarial basis for computing the rates of contributions required to assure a given range of benefits. Many societies fixed their rates too low and many became insolvent. From this unsatisfactory position the societies were rescued by the almost superhuman labours of a remarkable man, Henry Ratcliffe, secretary and actuary of the Manchester Unity Society from 1848 to 1877; and Ratcliffe's work was followed by that of Sir Alfred Watson, the first Government Actuary, whose analysis of the Manchester Unity experience during 1893–1897 was adopted as the foundation upon which the financial structure of the national health-insurance scheme was erected. Mr. Harris describes the scheme in detail and subjects it to a critical examination, from which it emerges with the conclusion that, though it has not done all that was expected of it, it "has brought about some very definite achievements" and has justified its existence as a precursor of a more comprehensive system.

The second part of the book considers the work of the insurance medical service set up by the Act of 1911, which was a very different thing from what was originally proposed for the medical care of the insured persons. The Bill as introduced into Parliament placed the administration of medical benefit in the hands of the approved societies, thus following the example of the german scheme, on which the british scheme was originally based. At the insistence of the British Medical Association, the Bill was drastically altered to give effect to the basic principle adopted by the Association—namely, that the conditions of insurance medical practice should closely approximate to those of private practice. To this end the Bill, as amended, transferred the administration of medical benefit from the approved societies to specially-constituted insurance committees, each containing representatives of the medical profession, and provided that every registered medical practitioner should have the right to undertake the medical care of insured persons under the scheme, that the insured persons should have the right to choose, and change, their insurance doctors, and that the medical profession should take part in the administration of the scheme. These alterations secured the coöperation of the doctors from the outset; though before medical benefit came into operation, unfortunate disputes had arisen between the Government and the doctors owing to misconceptions that might have been avoided. The British Medical Association, so far from desiring the abolition of medical benefit, has repeatedly urged that it should be extended to include the medical care of the insured persons' dependants and the provision of specialist services.

Mr. Harris gives an informative account of the working of medical benefit. He explains the difficulties against which both administrators and doctors have had to contend, and lays stress upon those arising from the limitation of the medical care provided for insured persons to such services as can properly be rendered by general practitioners. His book, well-written and free from technicalities, is a valuable contribution to the literature of health insurance, and is of special interest at the present time, now that the functions hitherto fulfilled by the national health insurance scheme are about to be widely extended.

G. F. McCleary

1083 Health and Social Welfare, 1947

Advisory editor *Lord Horder*. London, Todd Publishing Company, Ltd., 1946. 527 pages; 1 plate. 22 x 14 cm. £1 1s. [£1.05]

This is the third appearance of the annual reference book, *Health and social welfare*, and the time is opportune for a study of its value. In general this new edition for 1947 follows the plan of its predecessors. Section 1 comprises a series of short articles on medico-social topics; section 2, legislation and policy; section 3, official directories [i.e. directories of official bodies]; section 4, official statements [i.e. statements by official bodies]; section 5, unofficial statements [i.e. official statements by unofficial bodies]; section 6, officially-appointed committees and reports; section 7, careers in health and social welfare; section 8, directory of organizations interested; section 9, statistics and tables; section 10, books, periodicals and films; section 11, who's who in health and social welfare.

The table of contents is impressive, and at a first glance the reader will imagine that he has here a reference book for the public health services which will make unnecessary any further consultation of *Who's who*, *Whitaker's almanack*, or the *Medical directory*. But unfortunately a more careful examination discloses that *Health and social welfare*, 1947, is not so comprehensive as it appears and claims to be. The short articles in section 1 might well be omitted, as they are rather out of place in a reference work of this kind. The official directories of section 3 have made a bold attempt to be international (incidentally, although UNRRA appears, there is no mention of the Health Division); but why should Belgium be included and not France, why Southern Rhodesia and not Uganda or any other of the african colonies?

Startling omissions are to be found in section 5, "unofficial statements". The Lister Institute of Preventive Medicine is included, but neither the Oxford Institute of Social Medicine nor the London School of Hygiene and Tropical Medicine (nor is the London School of Hygiene Library included in the list of libraries on pp. 476-478); the Leeds Joint Council on Industrial Medicine, but not the Society of Industrial Medical Officers. Similar criticism could be levelled against section 8 but enough has been said already to indicate that in the reviewer's opinion the selection of organizations to be represented has been made haphazardly. This may perhaps arise from the fact that the publishers have tried to cover too wide a field. In attempting to cover both the fields of public health and social welfare, they have been unable to cover either adequately from the standpoint of essential reference material.

When we come to section 10, books, periodicals and films, the same haphazard selection is evident. Obviously, the book-list in such a volume, as the editors explain, is not intended to be exhaustive. But it could at least have been authoritative, or the basis of selection could have been made plain. Any value that the present list might have had is lost through the inclusion of much worthless, unorthodox and trivial literature. There are also far too many errors in the bibliographical data. Authors' names are misspelt; the same work appears under different authors; the *Quarterly cumulative index medicus*, which has appeared under its present title for nearly 30 years, appears as the *Index medicus*; while one entry: Smith, M. *Introduction to industrial nursing*. (Cassell) 1943, 7s. 6d., is simply incorrect, as there is no work with such a title by this author. Similar criticism could be levelled against the selection of periodicals. The most surprising omission here is that of the *Bulletin of Hygiene*, an invaluable abstracting periodical covering world literature on public health and related subjects.

With more careful editing, *Health and social welfare* could be a most valuable work of reference. It assembles a mass of useful information, for which search has usually to be made through numerous other works; but the principal need is for a definite basis of selection of the assembled material. The reviewer would like to see included in future editions a list of the university departments, with their personnel, concerned with public health and allied subjects, and details of the various MRC units, while the book and periodical lists should either be omitted entirely or thoroughly overhauled by a competent librarian with a sound knowledge of the literature of public health and social welfare.

H. A. I.

1084 A Handbook for Assistant Medical Officers of Health on Child Welfare and School Health Work

F. J. G. Lishman. Second Edition. London, H. K. Lewis & Co. Ltd., 1946. 89 pages. 22 x 14 cm. 7s. 6d. [£0.375]

Introduction. Maternity and child welfare centres; school health service. Appendices. Index.

A second edition of this little book has been made necessary by the changes imposed by the Education Act of 1944 and subsequent regulations made under this Act. The opportunity has been taken, with great advantage to the usefulness of the book, to extend the section on child welfare and especially to give a description of the work of child-welfare centres. Originally the material was used as a handbook for new Assistant County Medical Officers in Devonshire, where Dr. Lishman is Deputy. It would indeed have been unfortunate if it had not been made available in handbook form to all engaged in child-health work. It should serve another purpose, which the author probably did not foresee, and that is to give an insight to the new specialists, whose work will be so closely tied with the child-health programmes of local authorities, into the everyday work of these services.

It is pleasing to find at the very beginning of the book a plea for greater use to be made of the great amount of useful material available for proper statistical analysis in this kind of work, where records are being accumulated of the health, and departures from it, of the whole child population.

The book itself is in two sections—maternity and child-welfare centres and the school health-service. In the first of these, there is a brief description of the usual procedure, followed by a section on infant feeding and the usual difficulties encountered both with mother and with child. This is a plain account and is representative of the best practice in british child-welfare centres. The same can confidently be said of the section on the common disorders of infancy, including difficulties originating in emotional struggles between parent and child, and throughout the whole section from beginning to end, the essentially educative function of the centre is stressed.

The portion of the book devoted to the school health-service follows the same plan. It includes an excellent summary of current practice in school inspection, which mentions the stages in school life at which the children are thoroughly examined, and the system of follow-up with re-examinations of children known to suffer from disability. The action to be taken when it is decided after examination that the child requires some treatment must vary considerably according to custom and facilities in different areas, and the account given here is not so representative as in other sections of british practice.

In a balanced outline of the comprehensive routine physical examination, it is surprising to find the statement that "the otoscope in Periodical Medical Inspection detects a larger number of important defects than does the stethoscope, and may therefore be considered of greater value as a diagnostic instrument." We may forgive Dr. Lishman this eccentricity in view of the great interest which he takes in aural disease and of the value of his repeated writings on its neglect.

The section on handicapped pupils outlines the categories laid down by the Ministry, the procedure of ascertainment and certification, and the regulations concerning the special educational treatment to be provided for the various types and degrees of disability. There is a short account of the extent of the enlargement of the scope of treatment to be provided by education authorities under the new Act, and of the possible methods of integrating arrangements with those made under the National Health Service Act.

Finally there is a most useful appendix giving specimen forms for administrative and recording purposes, and typical informative educational leaflets for issue to parents.

For anyone overseas who wishes to understand the day-to-day child-health work of british local authorities, this little book can confidently be recommended as the best available.

A. C. Stevenson

[1029] How Britain was Fed in War Time: Food Control 1939–1945

Ministry of Food. London, His Majesty's Stationery Office, 1946. ii + 66 pages. 24 x 15 cm. 1s. [£.05]

(i) The wartime food shortage; (ii) the planning of food supplies; (iii) the economy of national resources; (iv) the machinery of food control; (v) food and the consumer. Appendices.

[For review, see *BMB* 1029.]

[1030] On the State of the Public Health during Six Years of War. Report of the Chief Medical Officer of the Ministry of Health, 1939–45

Ministry of Health. London, His Majesty's Stationery Office, 1946. iv + 280 pages. 25 x 15 cm. 5s. [£0.25]

Introduction. (i) Vital statistics; (ii) general epidemiology; (iii) emergency public health laboratory service; (iv) maternity and child welfare; (v) food and nutrition; (vi) emergency medical service; (vii) civil defence casualty service; (viii) problems of medical man-power; (ix) dental services; (x) the nursing services; (xi) morbidity statistics; (xii) advances in therapeutics; (xiii) international health and medical intelligence; (xiv) environmental hygiene; (xv) health publicity; (xvi) planning for the future. Appendices.

[For review, see *BMB* 1030.]

[1032] First Annual Report, 1945

Institute of Social Medicine, Oxford. 20 pages. 21 x 14 cm.

(i) (Introduction); (ii) accommodation; (iii) staff; (iv) purposes of the institute; (v) research programme and other current activities; (vi) teaching; (vii) publications; (viii) summary and discussion; (ix) relations of the Institute with Public Health authorities and others; (x) relationship of the Institute and the Bureau of Health and sickness records; (xi) visitors; (xii) programme for 1946; (xiii) changes in the Committee.

[For review, see *BMB* 1032.]

[1034] Interim Report of the County Medical Officer of Health and School Medical Officer for the Year 1945

London County Council. London, London County Council, 1946. 64 pages. 25 x 17 cm. 2s. [£0.1]

(i) Introduction; (ii) vital statistics; (iii) general public health; (iv) hospitals and ancillary services; (v) London ambulance service; (vi) school health service; (vii) mental health services. Index.

[For review, see *BMB* 1034.]

SURGERY

1085 La Apendicitis en la Primera Infancia

Jaime Damianovich & Alfredo Vidal Freyre. Buenos Aires, Editorial Ilustración Rioplatense, 1945. 231 pages; illustrations. 23 x 16 cm.

(i) Historia; (ii) etiopatogenia; (iii) anatomía del ciego y del apéndice; (iv) anatomía patológica; (v) bacteriologia; (vi) cuadro clínico; (vii) sintomatologia; (viii) diagnóstico; (ix) formas clínicas; (x) diagnóstico diferencial; (xi) evolución y pronóstico; (xii) complicaciones; (xiii) tratamiento; (xiv) intervención quirúrgica; (xv) apendicitis crónica; (xvi) síntesis final; (xvii) casuística propia; (xviii) casuística argentina. Bibliografía argentina. Bibliografía extranjera.

This clearly printed and well-illustrated book has for its object the countering of the general belief that appendicitis in young infants is very rare and very serious. It is based upon a close study of 61 cases of which 53 occurred in infants under two years of age. They note that the condition is often associated with general infection, especially influenza, and consider that if pain and tenderness in the appendix-area point to inflammation of the appendix it should be treated as a surgical condition. Four-fifths of their cases showed only catarrhal inflammation of the appendix, and this certainly supports the general view that the graver forms of appendicitis are rather uncommon in early infancy. The fact that operation was undertaken early in all these cases perhaps discounts the last-mentioned conclusion.

The authors stress the difficulties of diagnosis and the need for a complete examination in every case; yet they state that they only exceptionally make a rectal examination. In diagnosis they regard spontaneous pain and pain on local pressure as the chief indications of the complaint, but differential diagnosis is fully discussed. Early operation is advised when once the condition has been diagnosed. Operative technique is discussed by Dr. Adolfo Caballero and Dr. August Wybert; they prefer open ether as anaesthetic and use a modified McBurney's incision. The infant is allowed to be taken home on the second or third day after operation.

General rules for after-treatment are given. Only two of the 53 cases died. A full record of each case is appended and there are many illustrations showing the microscopical appearance of the removed appendix. There is a bibliography at the end.

This monograph deals thoroughly with a difficult subject, and is well worth perusal and study. Readers will probably vary in their opinion as to the urgency of the need for operation in some of the cases, but that very fact should stimulate them to observe their own cases more closely.

V. Zachary Cope

1086 Minor Surgery (Heath: Pollard: Davies: Williams) for the use of House Surgeons, Dressers, and Junior Practitioners

Cecil Flemming. Twenty-third edition. London, J. & A. Churchill Ltd., 1946. viii + 406 pages; 209 illustrations. 19 x 12 cm. 14s. [£0.7]

(i) Introduction; (ii) asepsis and antisepsis; (iii) preparation of the patient for operation—the operation; (iv) post-operative treatment; (v) wounds, contusions, burns, accidents, foreign bodies; (vi) haemorrhage; (vii) genito-urinary diseases; (viii) acute abdominal conditions, hernia and scrotal swellings; (ix) minor operations; (x) minor operations (continued); (xi) special dressings, strapping, bandaging; (xii) fractures; (xiii) special fractures, dislocations; (xiv) splinting of joints; (xv) administration of anaesthetics. Index.

This handy little volume provides an excellent guide to the senior student or junior graduate. As in similar books, the title "minor" surgery is capable of wide application, and it is easy to criticise such a book on the grounds of commission or omission. The author has exercised commendable judgement in his interpretation of the phrase.

The following are some points which call for consideration in the next edition. Sodium morrhuate is recommended as the best preparation for routine use for the injection of varicose veins. Allergic and anaphylactic reactions are now well recognized, and in 1942 the Council on Pharmacy of the American Medical Association recommended withdrawal of the 10 % solution. We doubt whether drainage of a bone-cyst conforms to modern ideas, as packing the cavity with bone-chips is now more or less universally practised. That most urgent and formidable operation—tracheotomy—is described in commendable detail, but we doubt whether the surgeon need worry about the thyroidea ima artery in the high operation.

Taxis is rather roundly condemned as a measure for the relief of a strangulated hernia. Bowel should not be further damaged unless excessive force is employed, and if circumstances are such that delay in operating is unavoidable, taxis properly applied to a previously reducible inguinal hernia is well worth consideration.

We doubt whether the author really believes that tightly compressing the limb by means of handkerchiefs will occlude the arteries. This is the treatment recommended for an adder-bite, and if arterial occlusion is considered necessary, an improvised tourniquet, described in a previous chapter, should be advocated.

"Tumour" is usually reserved for new growths, and the term should not be applied to the swelling which results from an intussusception.

For the operation of circumcision in infants, the simple and widely applied procedure of crushing the foreskin with bone forceps should be recommended. Surgeons familiar with this method use no other, and the risk of post-operative bleeding is eliminated. A serious omission in the chapter on post-operative treatment is a description of acute dilatation of the stomach—for the want of a little knowledge regarding this condition a patient may easily slip through the hands of an unsuspecting junior surgeon. Also the outlook in a case of hiccough need not be considered as grave until blocking of the left phrenic nerve by local anaesthesia has failed to relieve the condition.

The chapter on anaesthetics is excellent, and contains a full and practical description of all the methods which are commonly employed.

The index is meagre—less than six pages of large print widely spaced. A more complete index would undoubtedly be appreciated by readers.

The above criticisms detract but little from the value of the book, which can be warmly commended to those for whom it was written. It is easy to read, and contains a wealth of information imparted in a pleasant and practical manner.

1087 Surgery of the Hand

R. M. Handfield-Jones. Second edition. Edinburgh, E. & S. Livingstone Ltd., 1946. xii + 164 pages; 104 illustrations. 25 x 18 cm. £1

Section I: Infections of the hand. (i) Introduction and general principles; (ii) distal segment of the fingers; (iii) lymphangitis; (iv) infections of the tendon sheaths; (v) infections in the palm; (vi) involvement of the forearm; (vii) some less usual conditions; (viii) complications of infections of the hand; (ix) restoration of function. Section II: Injuries of the hand. (x) Fractures of phalanges and metacarpals; (xi) injuries to soft parts; (xii) amputations; (xiii) burns. Section III: Other surgical lesions. (xiv) Congenital and acquired defects; (xv) tumours. Index.

The grave results of faulty diagnosis and treatment of injuries and infections of the hand have been the subject of much emphasis and teaching during the past 25 years but, in spite of this, there is still, in general, a considerable lack of appreciation of its importance and an acceptance of poor functional results as inevitable. Kanavel's well-known monograph on the subject is the standard treatise but, as the author of the book under review points out in his preface, "the clinical treasures are overladen with experimental work" which detracts from its value as a practical guide, and for this reason Mr. Handfield-Jones' book, with its emphasis on principles and concise statement of practice, is of great value.

As the title indicates, the book is a treatise on all aspects of the surgery of the hand and, though more than half of it is devoted to the important subject of infection, it also covers other aspects of the subject, including fractures and burns. Since the first edition, the experiences of wartime have produced new ideas and methods, many of which have been incorporated into the new edition now published.

The approach to the subject is essentially practical, with emphasis on the broad principles of preservation and restoration of function, and the author has a concise and pleasant style which makes the book easy to read and assimilate. The principles of surgery are laid down and applied to the various problems under discussion—with a repetition of the warning easily forgotten by those growing up in the present age of chemotherapy that there is still the need for good surgery.

The description of each condition is full and concise. In this connexion it might be suggested that, in future editions, extended use might be made of short tables of signs and symptoms, such as that used in describing the differential diagnosis between distal-pulp infection and acute lymphangitis of the finger-end. If this were applied also, for example, to the description of the differential diagnosis between subcutaneous and tendon-sheath infection, it would enhance the value of the book for ready reference without in any way detracting from its merit as a textbook.

Treatment is clearly described and well-illustrated, and there are useful sections dealing with preventive measures and after-treatment. With regard to the latter, the short notes on the various forms of physiotherapy are helpful. It is probable that a fair proportion of doctors, especially the younger ones, who refer their cases to the massage or electrotherapy department, have not a very clear idea of what really happens to them when they get there.

As is proper in a book which is primarily intended as a practical guide to the general practitioner and house-surgeon, only one method of treatment is described in most instances. This will not be enough for those attempting the higher surgical examinations, who must be prepared to discuss the merits of several treatments with the examiner, but they would be well advised to obtain their basic ideas from this book.

The book is well produced, printed on good paper and excellently illustrated. It can be strongly recommended to those for whom it is written, the general practitioner and the house-surgeon, while the practising surgeon and the candidate for a higher surgical qualification can get much help and good advice from it.

J. W. S. L.

1088 Injuries and Diseases of the Oesophagus: being the George Haliburton Hume Memorial Lectures

G. Grey Turner. London, Cassell & Co., Ltd., 1946. 100 pages; 27 illustrations. 22 x 14 cm. 15s. [0.75]

(i) Introduction; (ii) examination and diagnosis; (iii) congenital anomalies; (iv) diverticulae or pouches; (v) foreign bodies; (vi) injuries; by corrosives; the result of instrumentation; external trauma; (vii) the management of mediastinitis; (viii) non-malignant stricture; (ix) achalasia or cardiospasm; (x) peptic ulcer and inflammatory conditions; (xi) non-malignant tumours; (xii) malignant disease; (xiii) miscellaneous. Conclusion. References. Index.

This work is the book-form of the George Haliburton Hume Memorial Lectures of 1943. The author's modest preface disclaims any intention to produce a complete account of the subject, but it becomes clear on opening the book that this is a masterly account and is the result of over forty years' unrivalled interest in and experience of the oesophagus.

Practically every lesion which may affect the oesophagus is dealt with at some length and is exemplified by case-report of the author's own patients. This characteristic is perhaps the hall-mark of the book. Nothing is recommended which has not been fully tried, no statement is made which is not amply supported by a brief note of some illustrative case.

The case-notes are short but the literary style is such as to make a great impression on the reader. "Many years ago . . . I was the very junior member of a trio who drove out from Newcastle in a carriage and pair one Sunday morning . . ." How refreshing are these well-rounded phrases—compare them with some of the breathless, illiterate and ill-considered writings which are only too common today.

These instructive case-accounts will fascinate and enthuse even the most apathetic reader. The book is well illustrated and includes some photographs and drawings of very remarkable specimens. Fifteen shillings seems a high price for a book of under a hundred pages, but the quality amply makes up for the quantity. This book can be confidently recommended, not only to surgeons who are concerned with the management of oesophageal conditions and who will find the greatest help in its pages, but also to general practitioners who have the responsibility of seeing the patients early and determining their fate. A perusal of this book will be invaluable to them—and, if its advice is followed—to their patients also.

R. H. F.

TEXTBOOK OF MEDICINE

1089 Textbook of Medicine by Various Authors

Edited by *Sir John Conybeare.* Eighth edition. Edinburgh, E. & S. Livingstone Ltd., 1946. xx + 1,170 pages; 66 illustrations. 22 x 14 cm. 30s. [£1.5]

Infectious diseases; tuberculosis; venereal diseases; tropical diseases; diseases due to metazoan parasites; diseases of infants; poisonings and intoxications; disorders of the endocrine system; diseases of metabolism; diseases of the blood, spleen, and lymphatic glands; diseases of the alimentary canal; diseases of the liver, gall-bladder, pancreas, and peritoneum; diseases of the cardio-vascular system; diseases of the respiratory system; renal diseases; affections of the joints and bones; diseases of the nervous system; psychological medicine; common diseases of the skin. Appendices. Index.

Of the popularity of this book among students, particularly of recent years, there can be little doubt. First published in 1929, this is the fourth edition to appear since 1939, and of these, two editions have had to be reprinted. The reason for this is not far to seek. The book is smaller than most textbooks of medicine, the style is clear and the teaching is dogmatic. Whether the student is the best judge of what is good for him may be debatable, but the demand for such a textbook clearly existed and in meeting the demand the distinguished editor of this work has been wholly successful. As it is only eighteen months since the previous edition was published, little radical revision has been considered necessary. The section on tropical diseases and endocrinology have undergone the most radical revision, and a useful addition is an appendix on aviation medicine. A section has also been added on the use of penicillin.

While the teaching is inherently sound, as is only to be expected from the high standing of the team of contributors from the London teaching hospitals whom the editor has collected around him, it cannot be said to be inspiring. The authors, or editors, of english textbooks seem to be incapable of appreciating that dullness and learning are not necessarily synonymous. The practice of medicine is a living subject and if the student is to be inspired with the humanity and humanism of his future career it is essential that his teaching should be humanistic and inspired, and not merely the dull recital of facts divorced from the drama that underlies that doctor-patient relationship of which we are hearing so much these days. Sir William Osler may have had his defects, but his name will always

Continued at foot of page 100

Shorter Notices

Air Ministry. Principles of anatomy and physiology for physical training instructors in the Royal Air Force

London, His Majesty's Stationery Office, 1946. vi + 180 pages; 158 figures. 25 x 16 cm. 7s. 6d. [£0.375]

The purpose of this manual issued by the Medical Services of the Royal Air Force is to explain certain important principles of anatomy and physiology which are particularly relevant to physical fitness. Chapters I–IV deal with anatomy and physiology, the emphasis being on the functional rather than on the theoretical aspects. In chapter V, posture and corrective exercises, and VI, breathing, reasons for the particular exercises are stressed rather than any specific methods or detailed lists of exercises. Chapter VII deals with mental and physical fatigue and fitness for flying; and chapter IX, with the rehabilitation of medical and surgical cases, describing the general methods and grading of remedial activity. The last part of this chapter contains a short description of some of the common pathological conditions seen at rehabilitation centres. The final chapter attempts to answer some of the common and more important questions asked by physical-training instructors. This work, which stresses the close relationship of anatomy and physiology to physical training, should prove valuable to all instructors as well as to others engaged in physical rehabilitation.

Demonstrations of physical signs in clinical surgery

Hamilton Bailey. Tenth edition. Bristol, John Wright & Sons Ltd., 1946. xii + 375 pages; 573 illustrations. 23 x 15 cm. £1 10s. [£1.5]

Once again this new edition of one of the most successful works on surgical diagnosis has been considerably revised. The author has still rigidly adhered to his original idea that the book should convey demonstrations of actual cases, and has brought before the reader many new patients. It is a tribute to the thoroughness and care of the author that he can state in his preface that every one of the 573 illustrations has received individual scrutiny.

This work has now required 10 editions and 7 reprints since it first appeared in 1927; german and turkish editions have appeared; spanish, portuguese, italian and greek are in active preparation; and a dutch edition is being negotiated. We can, therefore, say with truth that Bailey's *Physical signs in clinical surgery* has an international reputation.

Pye's surgical handicraft

Edited by *Hamilton Bailey.* Fifteenth edition. Bristol, John Wright & Sons Ltd., 1947. xii + 668 pages; 789 illustrations. 23 x 15 cm. £1 5s. [£1.25]

Over sixty years have passed since the first publication of *Surgical handicraft* by Walter Pye, and of the fifteen editions which have appeared, Hamilton Bailey and his team of eminent contributors have been responsible for the last five. Of the popularity of this work there can be little doubt, for it has served the needs of successive generations of house-surgeons and practitioners.

The object of "Pye" is the same today as it was in 1884, to indicate and illustrate the principles of craftsmanship in minor surgical procedures and manipulation. But if it is to continue to be used with the same confidence, then the work has to be revised thoroughly every few years. In this new edition, by re-arrangement, by revision, by additions, every effort has been made to bring the work thoroughly into line with modern technique, and it can safely be said to represent the best british teaching. A feature of the work is the use of many illustrations, some of them in colour, to present pictorially technical procedures.

El colapso circulatorio

A. Curieses del Agua. Mahón, Imp. M. Sintes Rotger, 1946. 238 pages. 22 x 16 cm. Ptas. 45.00

This book deals firstly with the mechanics of circulation and defines the term collapse. The author studies the different types of collapse and the causes and diagnosis of each. A chapter deals with the treatment of collapse by [so-called] mechanical methods, e.g. by transfusion of human blood and heterologous plasma, as well as by surgical means. An account is given of the morphological and physico-chemical alterations which follow collapse, and separate sections are devoted to descriptions of the renal, hepatic, intestinal, pancreatic, cerebral, cardiac and muscular changes which occur. A further section deals with the prevention of collapse. The author also considers the frequency of collapse with reference to sex and age and to predisposing congenital or acquired factors. He emphasizes the need for knowledge on the part of the physician or surgeon of his patients' constitutional make-up and history.

Psychological medicine: A short introduction to psychiatry

Desmond Curran & Eric Guttmann. Second edition. Edinburgh, E. & S. Livingstone Ltd., 1945. viii + 246 pages; 20 illustrations. 22 x 14 cm. 10s. 6d. [£0.525]

This book, the first edition of which appeared in 1943, is a useful addition to psychiatric literature. It enables the practitioner to familiarize himself with the more practical aspects of psychiatry, and for more intensive study contains a good annotated bibliography.

The new edition has been extensively revised, and a number of sections and chapters have been rewritten and enlarged. The principal alterations and additions were made in the sections on constitutional factors and psychopathic personalities and in the chapters dealing with the affective and hysterical syndromes. Some of the problems of psychosomatic medicine have been briefly discussed, while an entire chapter has been devoted to obsessional states. The appendix on "Psychiatry in war-time" has been retained, as the authors believe that many of the important stresses of war are likely to continue in the postwar world. The book is well produced and contains some excellent illustrations.

Textbook of medical treatment by various authors

Edited by *D. M. Dunlop, L. S. P. Davidson and J. W. McNee.* Fourth edition. Edinburgh, E. & S. Livingstone Ltd., 1946. xix + 923 pages; 38 illustrations. 24 x 17 cm. £1 10s. [£1.5]

In the fourth edition of the scottish school's deservedly popular *Textbook of medical treatment*,

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TEXTBOOK OF MEDICINE

Continued from page 99

rank high in the annals of medical history because of his skill in presenting medicine as a living subject.

Apart from this general criticism, which, it should be added, is applicable to many contemporary textbooks, there are two specific ones. In the first place, apart from a few *x*-rays and electrocardiograms, there is a complete absence of illustrations. No amount of verbal description will ever convey to a student as impressive a picture of, say, thyrotoxicosis, Addison's disease or rickets as will a well-chosen photograph. The vast majority of medical students are picture-readers and not word-readers, yet how seldom does an english textbook make allowance for this. Then again, there is a certain lack of balance in the presentation of the subject. To devote more space to mucomembranous colitis than to Hirschsprung's disease, to dismiss threadworms in a mere dozen lines, and to devote more space to sarcoidosis than to acute bronchitis, is to give the student an entirely wrong outlook. Anorexia nervosa is a difficult condition to classify, but it is surprising to find it included here under "nervous dyspepsia" along with visceroptosis. There may have been a tendency of recent years to over-emphasize the importance of the endocrine glands, but it is surely swinging the pendulum too far in the opposite direction to devote merely 25 pages to endocrinology and 12 pages to vitamin-deficiency diseases in a book of some 1,150 pages.

Perhaps in preparing the next edition the editor and his contributors may find it possible to devote more time than has been possible during the last eight years to a radical revision of their book which will bring it more into line with modern views on the style, format and presentation of textbooks. Meanwhile we have little doubt that medical students, as well as practitioners, will continue to use it, and in so doing they can depend upon the soundness and the validity of the work.

USAGE OF DDT

[1031] Some Properties and Applications of D.D.T.

Ministry of Supply. London, His Majesty's Stationery Office, 1946. 34 pages. 24 x 15 cm. 6d. [£.025]

(i) General; (ii) physical and chemical properties of D.D.T.; (iii) general review of toxicity; (iv) D.D.T. formulations; (v) means of dispersal; (vi) toxicity to vertebrates; (vii) toxicity to arthropods. Bibliography. Appendices.

[For review, see *BMB* 1031.]

[1031] DDT: The Synthetic Insecticide

T. F. West & G. A. Campbell. London, Chapman & Hall Ltd., 1946. xii *h* 301 pages; 13 plates. 22 x 14 cm. 21s. [£1.05]

Prologue. History and development. Part I: (i) The Basle researches; (ii) manufacture and chemistry; (iii) principles of formulation; (iv) toxic manifestations; (v) DDT in paints and miscellaneous materials; (vi) DDT in textiles and paper; (vii) DDT miscellany. Part II: (viii) DDT against human lice; (ix) DDT against mosquitoes; (x) DDT against household pests; (xi) DDT against other pests affecting men and animals; (xii) DDT against plant pests; (xiii) miscellaneous uses of DDT; (xiv) effect of DDT upon beneficial insects and phytotoxicity. Epilogue. The way ahead. Author index. Subject index.

[For review, see *BMB* 1031.]

the format of the book has been changed. By using a slightly larger page the number of pages has been reduced, although the actual subject-matter has been slightly increased. Great advances have been made in the last few years in preventive and curative medicine, and their inclusion is necessary in any modern survey of therapeutic methods. But the editors have decided, and decided wisely in a work intended for the student and the general practitioner, that as the experience of some of the new drugs is still necessarily limited, the time has not yet come to omit entirely certain of the older methods of treatment. In this way, the new edition strives to reach a balance between the well-tried[1] old and the new methods of treatment.

A new chapter has been added on penicillin therapy. The sections on venereal diseases and diseases of the thyroid gland have been almost entirely rewritten, and the chapter on the diseases of the respiratory system has been extensively revised. Lastly, a short account has been given in a postscript of the new insecticide DDT.

Edinburgh post-graduate lectures in medicine

Vol. 3. Edinburgh, Oliver & Boyd, 1946. xi + 587 pages ; illustrations. 15s. [£0.75]

The Edinburgh School of Medicine was fortunate in being able to arrange for the delivery of post-graduate lectures at regular intervals throughout the war. The publication of this, the third volume, containing 32 lectures delivered between January 1942 and December 1943, has been delayed owing to the paper shortage. As with previous volumes, the lectures cover a wide range of subjects representing some of the many activities of the Edinburgh School, but we must agree with a reviewer in another journal, who questions the value of such a miscellaneous collection.

Vers l'infiniment petit

Armand de Gramont. 8me édition. Paris, Gallimard, 1945. 247 pages; 75 illustrations. 160 francs.

This study of microscopy by a member of the Académie des Sciences forms part of the collection *L'avenir de la science*, edited by Jean Rostand. The first chapter consists of a short essay on Van Leeuwenhoek, "the father of micrography," and his work. This is followed by an account of the evolution of the microscope from the time of Van Leeuwenhoek to the present day. Chapters III–VII deal respectively with the condenser, dark ground and ultramicroscopy, binocular microscopy, the metallographic microscope and the polarizer microscope. Chapter VIII, which deals with dissociation, staining and fluorescence, includes an account of Dr. P. de Fonbrune's micromanipulator, which was described in an earlier number of this Bulletin (see *BMB* 812). There follow chapters on photomicrography (including radiomicrography and cinemicrography), statistical photography, and interference. Chapter XII deals with Louis de Broglie's "onde associée" and the electron microscope, chapter XIII with bacteria, viruses and bacteriophages, and chapter XIV with disintegration and artificial radioactivity. The book is well illustrated with photomicrographs and diagrams. There is no index or bibliography, but some rather incomplete references are given in footnotes. In a work of this kind, these might, with advantage, have been more numerous and informative.

[1] [But the history of therapeutics shows plainly that the fact that a method is "well-tried" does not make it worthy of retention.—ED.]

Clinical practice in infectious diseases for students, practitioners and medical officers

E. H. R. Harries & M. Mitman. Third edition. Edinburgh, E. & S. Livingstone Ltd., 1947. xi + 679 pages ; 56 figures. 22 x 14 cm. £1 2s. 6d. [£1.125]

The second edition of this work was reviewed in an earlier number of the *Bulletin* (*BMB* 387/44), and in the new edition the whole text has been revised and new matter introduced.

New knowledge in the control and treatment of the acute infectious diseases is now being accumulated rapidly, and the authors have made every endeavour to ensure that the work is completely up-to-date. The chief addition is a new chapter on the pneumonias, and there are descriptions of the common cold, febrile herpes, epidemic nausea and vomiting, epidemic myalgia and infective polyneuritis. The account of penicillin has been considerably enlarged and a brief note added on streptomycin. Inevitably these additions have increased the size of the volume; it is now over 200 pages larger than the first edition published seven years ago. The student, the practitioner and the medical officer will find in it a valuable and up-to-date exposition of modern ideas on infectious diseases.

Pulmonary Tuberculosis

R. Y. Keers & B. G. Rigden. Second edition. Edinburgh, E. & S. Livingstone Ltd., 1946. xvi + 277 pages; 124 figures. 19 x 12 cm. 17s. 6d. [£0.875]

The publication of a second edition only one year after the first has shown the need for this concise account of the present knowledge of pulmonary tuberculosis. There has been no major development in this particular field of medicine demanding extensive additions of new material, but the opportunity has been taken to revise thoroughly the entire text, and certain sections, those on pathology, epidemiology and resistance, and BCG have been entirely re-written. The number of illustrations has not been altered, but some new *x*-ray plates have been substituted.

Aids to dermatology

Robert M. B. MacKenna. Third edition. London, Baillière, Tindall & Cox, 1946. viii + 309 pages ; 7 illustrations. 17 x 11 cm. 6s. [£0.3]

This short introduction to the subject has undergone extensive changes in the third edition. In particular, owing to the rapid growth in the knowledge of venereology, that subject could no longer be dealt with in a single chapter, and is now dealt with in a separate volume of the *Students' Aids Series*.

New material has been added and a good deal of revision has been undertaken in this new edition, but the work remains a volume for students and practitioners who require a synopsis of the commoner cutaneous diseases.

Practical anaesthetics for students, hospital residents and practitioners

J. Ross Mackenzie. Second edition. London, Baillière, Tindall & Cox, 1946. xii + 172 pages ; 71 illustrations. 22 x 14 cm. 10s. 6d. [£0.525]

The author of this short manual on anaesthetics, who is lecturer on anaesthesia in the University of Aberdeen, states in his preface that "No departure has been made from the original purpose of the handbook. It is intended as a guide to the elements of practical anaesthetics for students, hospital residents and practitioners and as a survey of the general knowledge in anaesthetics which the medical student should possess before graduation." This edition has been revised throughout and some additional matter included in several of the chapters with the object of elucidating the text.

You and your children. BBC talks by a woman medical psychologist

Ministry of Health. London, His Majesty's Stationery Office, 1946. 32 pages ; illustrations. 18 x 12 cm. 6d. [£0.025]

This is a paper-bound collection of short BBC talks by a medical psychologist, Dr. Doris Odlum, which, to quote the Foreword, " . . . give simple hints on the handling of normal children—their fears, fads and fancies—and the problems that arise in every family." Basic precepts of the psychology of young children, such as their need for a secure background and for affection, and the most common behaviour-problems, such as faddiness in eating, habit-training and disobedience, are discussed in the simplest terms, sometimes suspect of "talking-down" to the invisible audience. Rather unequal drawings by "Proops", which show children in the practical and make-believe activities of every day, break up the text. This booklet might be of help or interest to parents with little or unenlightened experience of children.

The M.B., B.S. finals

Francis Mitchell-Heggs. Third edition. London, J. & A. Churchill Ltd., 1947. xvi + 99 pages. 21 x 13 cm. 8s. 6d. [£0.425]

This work is intended for a student working for the final medical examination of London University. It consists firstly of extracts from the University regulations relating to degrees in medicine and surgery, and secondly of a collection of the questions set at the examinations for the years 1932-45, classified and arranged in suitable sub-divisions. As the London degree is recognized as setting a high standard in qualifying examinations, it is likely that this volume will be of use not only to the London student but to those taking the examinations of other british universities.

Pasteur

Henri Monod. Paris, Editions Correa, 1945. 189 pages ; 9 illustrations. 19 x 12 cm. 150 francs.

It is in some ways a strange idea that the anniversary of the death of a great man should be celebrated, but Pasteur was so great that it is perhaps as well that we should seek a convenient pretext for recalling his incomparable achievements. That, at any rate, has been the view taken in France, and one of the products of the 50th anniversary of Pasteur's death is a new short biography by Henri Monod. The author makes no claim to originality for his material, but he provides a readable account of the main features of Pasteur's life, work and spirit.

The author shows the versatility characteristic of many medical writers in the french and other latin languages. From the list of his other publications given on the fly-leaf it appears that his interests range from cancer of the rectum and gonococcal arthritis on the one hand, to the friendship between Verlaine and Mallarmé on the other hand.

Aids to the diagnosis and treatment of venereal diseases

T. E. Osmond. London, Baillière, Tindall & Cox, 1946. vi + 138 pages ; 4 illustrations. 17 x 11 cm. 5s. [£0.25]

This is a new volume in the familiar *Students' Aids Series*, and as explained above has been separated from the *Aids to Dermatology*. The author, who is honorary consultant in venereal diseases to the british army, has written this short

work chiefly for the medical student who needs some instruction in the management of venereal diseases.

Ocular prosthesis

J. H. Prince. Edinburgh, E. & S. Livingstone Ltd., 1946. viii + 134 pages; 76 illustrations. 23 x 14 cm. 17s. 6d. [£0.875]

What little literature in english previously existed on the making and fitting of artificial eyes was to be found only in periodicals, and we are indebted to the author for writing this work. After a short history of the development of artificial eyes dating back to 200 B.C. the author outlines the anatomical and physiological facts essential to an understanding of the requirements of an artificial eye. This chapter may need some revision in future editions, but the author is on safer ground in later chapters dealing with the fitting, the hygiene and the manufacture of artificial eyes. The work undoubtedly fills a gap in ophthalmic literature and will be most valuable, especially to artificial-eye makers.

Aids to public health

Llywelyn Roberts. Fifth edition. London, Baillière, Tindall & Cox, 1946. viii + 259 pages; 4 illustrations. 17 x 11 cm. 6s. [£0.3]

In the eight years which have elapsed since the previous edition of this little work by the Medical Officer of Health of Swindon, many advances both in the theory and practice of public health have occurred.

The basic conception of public health itself is changing with the emergence of social medicine. These imminent changes in practice will inevitably affect the students' curriculum for which this work is intended. But change as the curriculum may, the basic factors of adequate nutrition and healthy environment in the prevention of national ill-health cannot lose their importance, and these factors Dr. Roberts rightly stresses.

Esquisse d'une histoire de la biologie

Jean Rostand. 2me édition. Paris, Gallimard, 1945. 257 pages; 14 plates. 140 francs.

The author's object, in the present volume, has been to give a concise review of the evolution of biology from the middle of the 17th century to the present day. The term biology has been taken to comprise the three fundamental problems of the formation of the individual, the evolution of the species, and the genesis of life. M. Rostand has already published three separate volumes on the history of these three problems, and this work is here condensed and adapted to form a shortened, coherent account of the general trend of biological progress. Each chapter deals with an individual problem, theory or discovery, and gives an account of the work of the scientist or scientists particularly connected with them. The opening chapter deals with Redi, Leeuwenhoek and the microscope. Other typical headings are: The experiments of Spallanzani; Cuvier and the science of fossils; Charles Darwin and the *Origin of species*; Pasteur and so-called spontaneous generation; Thomas Hunt Morgan and the theory of the gene. A useful feature of the book is a list of the principal dates in the history of biology. There is also a short bibliography, in addition to references given in footnotes, and an index of names. The book is illustrated with portraits of some of the personalities whose work is described.

Histoire de la science

Pierre Rousseau. 23e édition. Paris, Librairie Arthème Fayard, 1945. 823 pages. 19 x 12 cm. 148 francs.

"L'histoire de la science, c'est la science même." This appropriate quotation from Auguste Comte appears at the beginning of Pierre Rousseau's *Histoire de la science*. M. Rousseau has written this 800-page work from the point of view of one who believes that the history of science is inseparable from the history of human thought. The book takes us from prehistoric times to the age of radioactivity and atomic physics. It is one of a large and valuable series—*Les grandes études historiques*—published by Librairie Arthème Fayard.

Aids to bacteriology

H. W. Scott-Wilson. Seventh edition. London, Baillière, Tindall & Cox, 1946. vii + 300 pages. 16 x 10 cm. 6s. [£0.3]

H. W. Scott-Wilson, Director of the Laboratories of Pathology and Public Health, London, revised this book by the late Mr. William Partridge for the sixth edition (1938). Since then, as he states in the preface to this new edition, "The intervening six years of war have again focused attention on the subject of wound infection, and great advances have been made in its treatment through the extended use of the sulphonamide group of drugs and the introduction of penicillin . . . The text has been completely revised . . ." After this preface, it is strange to find no entries in the index under, for example, Sulphonamides, Sulphapyridine, Sulphathiazole, or Chemotherapy; search reveals brief references to them in the text. The general description of penicillin is confined to 15 lines, which give nothing of its characteristics. No mention seems to be made of its use against spirochaetes nor actinomycosis (although the latter appears in the index), nor of the chemotherapy of malaria. Brief references to chemotherapy are scattered through the text. The information given is altogether insufficient to aid a student to answer an examination question on antibiotics, which would appear to come within the province of bacteriology. Moreover, no description is given of selective media for isolation of typhoid and dysentery bacilli; and the bacteriological nomenclature is sometimes archaic. As indicated already, the usefulness of the book for ready reference and revision, which would seem to be among its main objects, is very much decreased by the extraordinary incompleteness of the index, which requires extensive enlargement and revision. This member of the *Students' Aids Series*, if it is to be of value to the students for whom it is largely designed, should be revised by someone in immediate contact with their needs.

Diseases of infancy and childhood

Wilfrid Sheldon. Fifth edition. London, J. & A. Churchill Ltd., 1946. viii + 775 pages; 161 illustrations. 23 x 14 cm. £1 10s. [£1.5]

This work has now become one of the standard textbooks on paediatrics, and the new edition shows evidence of modifications and additions, some of them considerable, in every chapter. Since the previous edition the most noteworthy advance has been the discovery of penicillin, and in order to avoid frequent repetition a brief appendix on penicillin therapy has been added. Chapters and sections that have undergone the heaviest revision include prematurity and diseases of the newborn, intrathoracic tuberculosis, infective hepatitis, intracranial haemorrhage, coeliac disease, fibrocystic disease of the pancreas, and poliomyelitis, while experience of the surgery of patent ductus arteriosus has necessitated more than the original few lines on this deformity. The surgical outlook in relation to oesophageal atresia and chronic lung disease has required modification, while the place of bronchoscopy in intrathoracic tuberculosis has deserved mention. Four new plates and several new text figures have been added. This new edition of Sheldon will be welcomed by both the clinical student and the general practitioner.

Penicilina. Compendium din publicaţiunile engleze asupra penicilinei apărute dela 1929 până în 1946

Edited by *G. B. Shirlaw.* Bucharest, Editura Societăţii Române de Statistică Bucureşti, [1946]. 316 pages. 28 x 23 cm.

This collection of rumanian translations of abou 150 articles and abstracts on penicillin which appeared in british journals from 1929 to 1946 should be of great help in filling wartime lacunae in rumanian knowledge of english medical literature in this field. The editor, Major G. B. Shirlaw, of the British Mission, Rumania, also points out in his introduction that it is hoped that the literature thus made available will aid in solving the problem of administration involved in allocating the limited quantities of penicillin imported into that country.

The material has been arranged under the following main headings: Discovery of penicillin; preparation of penicillin, preliminary studies, laboratory methods; chemical properties of penicillin; pharmacology and experimental therapeutics; clinical uses of penicillin; surgical applications of penicillin; use of penicillin in medical affections; use of penicillin in special diseases.

An alphabetical index of authors gives the english and rumanian titles and the original references, but contains no cross-references under the names of joint authors. It would have been of help to rumanian bibliographers if the complete reference had been given in all cases: for many references the volume and/or page number is omitted. Moreover, while it would have added another burden to the already heavy task of the compilers, a subject index, even if it contained only the main subject headings, would have increased the value of the compilation for ready reference. Major Shirlaw's introduction, and the foreword, by Air Vice-Marshal D. F. Stevenson, Commissioner of the Mission, appear in both rumanian and english. In spite of the minor criticisms made above, and the presence of some typographical errors, this is a praiseworthy example of international co-operation in medicine. A sturdy loose-leaf binding has been adopted so that users can insert reprints and their own notes into the same volume.

El enclavamiento intramedular de Küntscher

C. Gil Turner. Madrid, Revista Española de Cirugía, 1946. 90 pages; 18 figures. 22 x 16 cm. Ptas. 25

This book is written by the clinical director of the casualty and orthopaedic department of the Provincial Hospital and of the Clinic of Pathological Surgery of the Faculty of Medicine, Madrid. The author and his colleagues were the first to apply in Spain Küntscher's method of intramedullary nailing in the treatment of fractures of the long bones, as explained by him at the German Surgical Congress in 1940.

The first section of the book gives a short historical sketch of the precursors of this method, from the time of Hippocrates. The remainder of the book deals with the mechanical and biological problems involved, possible complications and accidents which may arise, operative technique and technical difficulties which may be met with in carrying out the treatment. Finally, the author gives details of seven cases of fractures of the long bones dealt with successfully by this method. The book is illustrated with reproductions of *x*-ray photographs and diagrams, and a bibliography is included.

Books Received

December 1946—May 1947

Many of the books listed will be, or have already been, reviewed in the Bulletin

Abderhalden, R. *Vitamine, Hormone, Fermente.* 1946. Schwabe (Basle), Sw.fr. 14.50

Adrian, E. D. *The physical background of perception.* 1947. Oxford University Press, 10s. [£0.5]

Adriani, J. *The chemistry of anaesthesia.* 1946. Blackwell, 35s. [£1.75]

Air Ministry. *Psychological disorders in flying personnel of the Royal Air Force investigated during the war 1939-1945.* (Air Publication 3139.) 1947. His Majesty's Stationery Office, 7s. 6d. [£0.375]

Aleksandrodrowicz, J. *Schorzenia narzadów krwiotwórczych w świetle badán bioptycznych szpiku kostnego, śledziony i gruczołow chłonnych.* 1946. D. E. Friedlein (Krakowie)

Alvarez Sainz de Aja, E. *Lo que todo el mundo debe saber sobre la sífilis.* 1946. Gráficas Gonzalez (Madrid)

Alvarez Sainz de Aja, E. *La linfogranulomatosis inguinal subaguda o cuarta enfermedad venérea.* 1946. Gráficas Gonzalez (Madrid)

Appleton, A. B., Hamilton, W. J. & Simon, G. *Surface and radiological anatomy.* 2nd ed. 1946. Heffer, 31s. 6d. [£1.575]

Aschner, B. *The art of healing.* 1947. (Heinemann) Research Books, Ltd., 12s. 6d. [£0.625]

Australia Department of Health. *Spiders, ticks, and mites. Including the species harmful to man in Australia and New Guinea.* Section I. Descriptive . . . F. H. Taylor. Section II. Clinical . . . R. H. Murray. (Service Publication School of Public Health and Tropical Medicine No. 6, University of Sydney)

Bailey, H., editor. *Pye's surgical handicraft.* 15th ed. 1946. Wright, 25s. [£1.25]

Bailey, H. & Love, R. J. M. *Surgery for nurses.* 6th ed. 1946. Lewis, 21s. [£1.05]

Baldwin, E. *Dynamic aspects of biochemistry.* 1947. Cambridge University Press, 21s. [£1.05]

Barcroft, J. *Researches on pre-natal life.* Vol. 1. 1946. Blackwell, 37s. 6d. [£1.875]

Barton-Wright, E. C. *Practical methods for the microbiological assay of the vitamin B complex and essential amino acids.* 1946. Ashe Laboratories, London, 7s. 6d. [£0.375]

Berkeley, C. *A handbook of midwifery for obstetric dressers, pupil-midwives and midwives.* 13th ed. 1947. Cassell, 12s. 6d. [£0.625]

Bowley, A. H. *The psychology of the unwanted child.* 1947. Livingstone, 6s. [£0.3]

Branco Ribeiro, E. *Estudos cirúrgicos.* 4ª serie. 1945. Livraria Atheneu (São Paulo)

British Empire Cancer Campaign. *Twenty-third annual report 1946*

Brocher, J. E. W. *Die Scheuermannsche Krankheit und ihre Differentialdiagnose.* 1946. Schwabe (Basle), Sw.fr.11

Brompton Hospital. *Brompton Hospital Reports. Vol. XIV, 1945.* Brompton Hospital, 10s. [£0.5]

Brown, R. C. *Ulcer of the stomach, duodenum and jejunum.* 1946. Oxford University Press (New York), 12s. 6d. [£0.625]

Browne, F. J. *Advice to the expectant mother on the care of her health and that of her child.* 6th ed. 1947. Livingstone, 6d. [£0.025]

Browne, O'D.T.D. *The Rotunda Hospital, 1745-1945.* 1947. Livingstone, 42s. [£2.1]

Burnet, F. M. *Virus as organism.* 1946. Oxford University Press, 11s. 6d. [£0.575]

Burt, C. *Intelligence and fertility.* (Occasional papers on eugenics: No. 2.) 1946. The Eugenics Society and H. Hamilton, 2s. [£0.1]

Callow, A. B. *Food and health: an introduction to the science of nutrition.* 3rd ed. 1946. Oxford University Press, 6s. [£0.3]

Casanovas, M. *Tratamiento actual de la sífilis.* 1946. Colección Española de Monografías Médicas (Barcelona)

Castex, M. R. *Ciencia Británica.* 1946. Editorial Bajel (Buenos Aires)

Christie, A. B. *Infectious diseases: with chapters on venereal diseases.* 1946. Faber, 12s. 6d. [£0.625]

Clavero, G. *Aedinos de España.* 1946. Gráficas Gonzalez (Madrid)

Cohen, M. B. *Manual de alergia.* 1947. Colección Española de Monografías Médicas 61–62 (Barcelona)

Constam, G. R. *Leitfaden für Zuckerkranke.* 1947. Schwabe (Basle), Sw.fr.12.50

Conybeare, J. *Textbook of medicine.* 8th ed. 1946. Livingstone, 30s. [£1.5]

Cooper, J. W. & Dyer, F. J. *Preparação de medicamentos.* Vol. 1. 1946. Casa do Castelo (Coimbra)

Cox, L. B. & Tolhurst, J. C. *Human torulosis.* 1946. Oxford University Press (Melbourne U.P.), 25s. [£1.25]

Curieses del Agua, A. *El colapso circulatorio.* 1946. M. Sintes Rotger (Mahón)

Cuthbertson, D. P. *Report on nutrition in Newfoundland.* (Dominions Office. Dominions No. 4.) 1947. His Majesty's Stationery Office, 1s. 6d. [£0.075]

Darlington, C. D. *The evolution of genetic systems.* 1939, reprinted 1946. Cambridge University Press, 12s. 6d. [£0.625]

Denny-Brown, D. *Diseases of the basal ganglia and subthalamic nuclei.* 1946. Oxford University Press (New York), 12s. 6d. [£0.625]

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Films

1092

It's Up To You

made by Nettlefold Studios, 1946; owned by the Admiralty; 16 mm. sound, 560 feet [170 m.]; 35 mm. sound, 1,400 feet [420 m.]; black and white; 15 minutes.

This film was made by the British Navy for showing to sailors who have undergone orthopaedic treatment in hospital and are about to be sent on to one of the naval rehabilitation-centres. Most of these men have little idea of what such a centre is like or what is expected of them. The film shows the day-to-day routine of the centre and, of even greater importance, tries to convince the patients that the speed and completeness of their recovery depend very largely on their own efforts. It starts by explaining in simple terms that for a broken bone to repair itself the junction must be kept immobilized: this is the purpose of the plaster cast. Yet this immobilization must not extend to the neighbouring joints, otherwise the muscles which move over them will become rigid, and, what is more, glue will collect in the joints themselves and so the whole will set solid. Active movement of the joint will increase the blood circulating in the area, and the glue will be washed away. The purpose of the rehabilitation-centre is to put a man back to the job he came from; home-leave will not do that, for the temptation to take it easy will permit the solidifying process to get a hold and he will become crippled. At the rehabilitation-centre a patient will be medically examined on entry, and then given special treatments, graded gymnastics, and games to keep his limbs supple and guide them back to their old agility. The film explains that a patient cannot be a passive participant; he must take an active part in his own treatment if the centre is to achieve its aim and send him out fit for the job he came from—it's up to him!

This film, although obviously of special appeal to the navy, will be appreciated by orthopaedists and physiotherapists in all countries. It shows well how the british concept of rehabilitation envisages an active participation by the patient in his cure, and how the competitive team-spirit is introduced to enhance his keenness; how the doctors no longer treat their patients as diseases to be cured but as people who must be skilfully helped to cure themselves. The inclusion of an explanation why home-leave is not granted will be particularly appreciated, and altogether the film is commended both for its intent and content as an example of the new doctor-patient relationship which is gaining ground in postwar Britain.

B. S.

1093

Your Children and You

made by Realist Film Unit, 1946; owned and produced by the Central Office of Information for the Ministry of Health, in co-operation with the Central Council for Health Education; 16 mm. sound, 1090 feet [540 m.]; 35 mm. sound, 2,700 feet [810 m.]; black and white; 30 minutes.

This film is one of the series "Your Children's Ears", "Your Children's Eyes" and "Your Children's Teeth",[1] made for the Central Office of Information at the request of the Ministry of Health in co-operation with the Central Council of Health Education. It deals with the upbringing of children during their first few years of life.

First, the parents' interest and co-operation are won by a frank admission of the incessant "giving" they are called upon for the new member of the family. The suggestions start with the reminder that solid foods are much more easily introduced at the age of five months than at that of nine months. The child at this age needs a variety of toys and of things to look at around him. At one year, the motto given is "It's nice to be praised". A start can be made towards control of excretions, but complete control is not to be expected. A succession of fresh amusements at short intervals is necessary.

At 18 months, the motto is "More knowing than you think". The problems common at mealtimes are discussed in a constructive way. Parents are advised to encourage the small child to help in the housework and garden, it being admitted that the "help" is not very helpful. The common destructive habit of breaking up the home is to be met by giving the child a variety of things to do.

The occasion and methods of punishing are not ignored. The small child is taken to a bedroom and left there (but with the door open, for loneliness begets fear) or a favourite toy is removed for twenty-four hours (but not for longer). A nightlight will make going to sleep easier. A child who overhears an adult's remarks may not understand and appreciate the over-statements casually made. It is necessary to answer the child's question "where do I come from?" simple and directly, even if briefly, and when a new baby is coming the child must be encouraged to look forward to the new arrival, helping beforehand and when it has arrived. The inefficiency of casual threats, which are not put into effect, is noted, and the fact that most naughtiness is boredom.

This is an excellent film. "It sets an ideal, but the advice can be acted on without the parents 'growing wings'". The outlook is up-to-date, with emphasis on praise not blame, but it does not evade the need for punishment at times. It contains much material, and could well be seen by parents several times during the infancy of their child, and especially because much of the good advice is conveyed in a light way, by allusion rather than command. It could be shown to mothers waiting in the out-patient halls at children's hospitals and at antenatal and child-welfare clinics. A handbook giving the script with some stills as illustrations would be a most useful aid.

Ronald MacKeith

1094

Scabies—1946

made by New Realm Pictures, 1946; owned by Central Office of Information for Ministry of Health; 16 mm. sound, 920 feet [280 m.]; 35 mm. sound, 2,310 feet [690 m.]; black and white; 26 minutes.

The film "Scabies"[1] has been withdrawn and is replaced by "Scabies—1946". The old film has been re-edited and brought up-to-date, and some new material added.

The excellent close-ups of the mite, showing its habits and development, are followed as before by clinical cases showing the typical sites of infestation. Next comes a new sequence showing the range of drugs available for medication and their relative efficiency, and then are shown the methods of applying an emulsion of benzyl benzoate—the drug of choice. A short sequence on secondary infection is followed by an emphatic description of the needs for treating whole families rather than an individual as the infested unit. This new shortened version is an improvement on its predecessor, and is suitable for doctors, nurses and medical auxiliaries.

1095

Penicillin in Medical Practice

made by Realist Film Unit, 1946; owned by Central Office of Information for Ministry of Health; 16 mm. sound, 1,140 feet [340 m.]; kodachrome; 32 minutes.

The film is divided into three main parts—pharmacological properties of the drug, use in surgical conditions, and use in medical diseases.

In part 1 we are introduced to the parent mould; the pure drug is shown, its physical properties, acid-alkali stability, compatibility with other drugs, and destructibility by the enzyme penicillinase. Next are considered the organisms whose growth is inhibited by penicillin, its efficacy against these organisms, and the methods of testing their sensitivity. Then the various methods

[1] [For reviews, see *BMB* 956, 957, 958.—ED.]

[1] [For review, see *BMB* 796.—ED.]

of dispensing are shown: for surface-application; powder, spray, cream, eye-drops, and lozenges; and for systemic injection. Here follow instructions on the preparation of instruments for injection, and details of the techniques available: intramuscular with local analgesic, intramuscular suspension in oil, and intramuscular drip.

Part 2 shows penicillin used for traumatic surgery, burns, mastoid, whitlow, carbuncle and osteomyelitis. Part 3 considers pneumonia, empyema, meningitis, sub-acute bacterial endocarditis, Vincent's angina, impetigo, and varicose ulcer. This section is followed by a short reference to the use of penicillin in venereal diseases and then in ophthalmology. The film ends with a few warnings against abuse of this new drug.

This film is admittedly disappointing: it was intended to appear a year ago as an introduction to the use of the drug, but was delayed and has arrived too late to teach us anything new (so fast have the techniques of penicillin been adopted); the print-quality is poor, the image is jerky, and the captions are difficult to read in the english version. Yet it has its value, for the continual emphasis on the superiority of systemic over local application is good, and each of us will learn one or two more useful facts from the film. It is perhaps unfortunate that no reference is made to the possibility of inducing penicillin-resistant strains by underdosage.

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MEDICAL FILMS FROM AUSTRALIA

The New South Wales Committee in Postgraduate Medicine, centred in Sydney, has been for some time investigating the place that films could play in their work. Last autumn a library was started which now numbers over 50 films; these are gathered mainly from USA, with some from Britain and a few produced locally. A film librarian has been appointed, and there is a small preview-theatre attached. An ambitious acquisition-programme is arranged for 1947, and this Committee expects to become the central library in Australia for medical postgraduate teaching films. They have an exchange arrangement with the Scientific Film Association, by whose courtesy we are publishing the two reviews which follow.

1096

Neurological Sequelae of Deficiency Disease seen in ex-Prisoners-of-War

made and owned by New South Wales Committee in Postgraduate medicine, Sydney, Australia, 1945; 16 mm. sound, 700 feet [210 m.]; black and white; 17 minutes.

This shows the conditions found when Changi Camp was liberated, the cooking facilities, and the food. The dietary composition is analyzed, and then a series of cases is demonstrated. These show a wide range of lesions, including: pot-belly, foot-drop, neuro-muscular incoördination, retro-bulbar neuritis, aphasia, deafness, losses of skin-sensation, absent reflexes, and ankle clonus. This is a simple film which records usefully a wide variety of disorders of rare etiology.

1097

An Operation for Hydatid of the Liver

made at the Alfred Hospital Melbourne, for Johnson (Aspro) Proprietary, 1945; technical adviser Belcombe Quick, F.R.C.S.; 16 mm. sound, 600 feet [180 m.]; kodachrome; 14 minutes.

Laparotomy reveals multiple adhesions indicating rupture of the primary cyst at some time previously. Two daughter-cysts are detected and removed entire, the liver area is packed off, and the abscess opened. The fluid which pours out is aspirated, and then the mass of cysts is scooped out with a sharp long-handled spoon. After much work all remnants are removed, the cavity is dusted with sulphonamide, and closed by primary suture; it is filled with saline before the last stitch is tied. A drain is placed in the wound, which is closed. The two daughter-cysts first removed are opened: one is dead, but the other contains live cysts; a single bladder is examined, and then a single scolex. This film provides an admirably clear, concise and unhurried demonstration, and the commentary is in keeping. It will provide good teaching-material in countries where this disease is rare.

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SOME STRUCTURAL FEATURES OF THE MAMMARY TISSUES

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1 Embryonic, foetal and pre-pubertal development of the mammae
2 Development during oestrous (menstrual) cycles, pseudo-pregnancy
3 Development during pregnancy
4 The lactating gland
5 Involution
6 Some abnormal variations of growth and differentiation
7 Quantitative estimation of mammary growth
8 Connective-tissue stroma of the mammary gland
9 Mechanism of expulsion of milk
References

Contemporary accounts of the histology of the mammary glands are nearly always written in relation to the human breast. An outline of the well-known structural variations associated with intra-uterine life, puberty, pregnancy, lactation and involution is given, with perhaps some emphasis on the details of the so-called apocrine type of secretion, and on colostrum-formation. Such aspects as the relatively unimportant nerve-supply, and the clinically very important lymph-drainage, are usually included. An attempt will be made in the following account to focus on those structural details, regardless of their relevance to the human breast, which appear to be significant in current experimental work on mammary development and lactation. The experimental investigation of the mammary gland, whether confined to the endocrine factors responsible for glandular growth and the initiation and maintenance of secretion, or the origin of pathological conditions, including cancer, is complicated by the inherent variability of its tissues, without parallel in other organs of the body.

1. Embryonic, Foetal and Pre-pubertal Development of the Mammae

As is well known, these glands arise in the embryos of all mammals, including the Monotremes and Marsupials, from a slightly thickened area of ventral ectoderm extending on each side from the axilla to the inguinal region, distinguished in successive stages as the mammary band, and the mammary streak. This proliferation of surface-cells occurs irrespective of how many functional glands are to be developed, or where they may ultimately be located. From this stage, however, further growth is confined to the mammary lines, which mark out the distribution of the mammae peculiar to a particular species. In the sow, for instance, the mammary lines extend over the greater part of the mammary streak, but in man and bovines they are confined to the pectoral and inguinal regions respectively. With the appearance of mammary buds as localized proliferations establishing the points of origin of the primary ducts and the nipples in both males and females, and the disappearance of the intervening streak-areas, further development of the mammary glands follows closely the typical pattern of an exocrine gland. It is the extent and pattern of the post-natal phases of development which have been followed so closely in the numerous investigations of the endocrine factors controlling mammary growth (see Folley, 1947a).[1]

We may summarize the foetal and subsequent growth-phases as follows. One or more primary ducts, arising from the ingrowing ectodermal cells of the mammary bud, undergo repeated branching while extending away from the nipple-area into the connective-tissue stroma. These extensions will become the interlobar and interlobular ducts. Further budding from restricted lengths of the interlobular ducts results in the formation first of finer intralobular ducts, and then clusters of alveoli. Thus, the terminal budding of the duct-system determines the size and disposition of the lobules of the gland, as well as reducing or modifying the intervening stroma. In common with the accessory reproductive glands, and unlike the parotid or pancreas, these developmental stages are so slow that, until puberty, little more than the nipple with a system of primary and secondary ducts may be achieved (fig. 1, 2).

There are, of course, variations in different species in the precise mode of origin of the nipple, the appearance of extensive dilatations associated with the major ducts to form teat- and gland-cisterns, typical of the larger domestic mammals, and in the number of primary ducts opening on the surface of the nipple. The main features of development in various species, together with a full account of these variations, will be found in the valuable monograph by Turner (1939). A detailed account of the development of the human mamma is given by Dawson (1934).

Viewing the early developmental history from the experimental point of view, the following problems arise. What is the growth-behaviour of the mammary-bud tissue in the male and female during foetal life and infancy: does it respond, like the more mature gland, to hormonal stimulation? Are the immature epithelial components capable of secretory activity?

It is commonly assumed that the rudimentary mammary tissues are approximately the same in males and females at birth and that, until hormones stimulate their growth, there is no significant development from birth to puberty. Sex differences are distinguishable structurally in some species, however, even as early as the mammary-bud stage. In the cow, according to Turner (1930), the mammary buds in the female are of characteristic shape and are actually smaller than those in the male. Of more immediate importance is the recent discovery that there may be considerable variation in the extent of development of the immature mammary ducts later during the pre-pubertal phase, not only from one species to another, as has long been known, but within different strains of the same species. Richardson & Cloudman (1946) report variations in the degree of duct-development in nine inbred strains of male mice at 6-9 weeks. Possibly these differences may be

[1] [*BMB* 1100]

traceable even earlier, like those associated with sex differentiation in the bovine embryo.

It is obvious in connexion with the phenomenon of "witches' milk"[1] that the mammary-duct tissue proliferated during foetal life is sensitive to hormonal stimulation at birth. How early this sensitivity and secretory activity is acquired in the foetus does not appear to be known. Schmidbauer (1933) investigating the udder of the freemartin has shown, however, that male hormonal influences, sufficient to modify the genital system, leave the mammary glands unaffected, since the freemartin develops an udder indistinguishable from that in a normal virgin animal. The rudiments of the mamma in the foetus and the newborn possess, therefore, possible inherent genetical variations, and a sensitivity to hormonal stimulation at birth, if not earlier.

A third peculiarity of this immature tissue, already mentioned above, is its ability to undergo secretory activity, and this occurs in the absence of well-differentiated glandular tissue. It is a very common experience in histological preparations to find secretion of both protein and fat in the cells and lumen of the duct-system at almost any stage of development (fig. 8). Are we to regard this secretion as comparable with colostrum, for instance, which appears later when the gland is equipped with secretory alveoli? In this connexion there has been much argument concerning the transient lactation occurring at birth in human infants. Dawson (1934) regarded witches' milk as resulting from little more than the extrusion of desquamating epithelial cells from ducts canalized in the later months of foetal life. It is impossible, however, to ignore the many descriptions of a copious secretion containing fat-globules and other components of milk, which occurs in some infants at birth. Those who have denied that witches' milk is a true secretion have probably been reluctant to regard duct-tissue in its immature state as capable of forming a secretion in the absence of alveoli. Others have interpreted the terminal buds of the duct-system, which often appear to be lined by a single layer of epithelial cells, as transitory alveoli responsible alone for the secretion. As will be shown later, the precise identification of immature alveoli, as distinct from finer ducts and buds, is difficult, particularly in sections. It is now generally agreed that alveoli, comparable in form with the glandular units of the pregnant and lactating gland, appear only after repeated growth and extension of the duct-system, far in excess of what is present at birth (fig. 1). Although larger ducts possess an epithelial lining at least two cells in thickness, these can secrete some at least of the milk components, as Richter (1928) and others have shown from cytological examination. The mammary gland is not unique in showing secretory activity on the part of its duct-epithelium. Rawlinson (1935) has described secretory phenomena in the striated intralobular ducts of the salivary glands, but in this case it is not yet clear what constituents of saliva are released from this source.

It has been established so far that the proliferating ectoderm cells forming the duct-system of the mammary gland may possess inherent differences related to sex, strain and species, together with an early sensitivity to hormonal stimulation, including limited capacity for secretion. Before we attempt to follow the growth of the mammary gland postpartum, a digression must be made concerning techniques for the histological examination of the immature gland. A very incomplete, and often misleading picture of the growing ducts and alveoli during the immature or pregnant phases is obtained from the examination of thin sections taken from sample areas of the gland. The identification of developing alveoli may be uncertain in sections, and the full extent of the duct-system from the nipple to the terminal buds can be traced from serial sections only by some laborious method of reconstruction. By stripping off the skin of the mammary area, with the underlying ducts or glands in small animals such as the mouse, rat, rabbit and rhesus monkey, it is possible to fix the tissues while pinned out flat, and then to dissect off the skin. A simple staining with haematoxylin outlines the duct-system with great clarity, and the whole preparation can be mounted *in toto* (fig. 2, 3). This technique, first introduced by Lane-Claypon & Starling (1906), was used by Ancel & Bouin (1911) in their studies on the rabbit, since when it has undergone various modifications, notably by Dubois (1941) who describes in detail the precautions necessary for preparing whole mounts of all the mammary glands of a laboratory animal like the mouse, in a condition suitable for quantitative measurement. The value of the whole-mount method has also been recognized by pathologists in tracing the origins and development of mammary diseases, particularly in rodents. There are limitations to the method, particularly where the density of the tissues becomes too great, as for instance in late pregnancy; or in earlier stages where the shape (e.g. guinea-pig) or size of the mamma render it impossible to make a flat preparation. Unfortunately the larger mammae of cows, goats, sheep and humans must be examined in sections, in whole-mounts of rather restricted areas, or by thick slices. Methods for cutting rough serial slices, ranging from 0.5–5 mm. in thickness, using an electrically-driven meat-slicing machine, are described by Ingleby & Holly (1939) for the human breast, and by Schalm & Haring (1939) for the udders of bovines. It is not sufficiently realized by some pathologists that thick (100 μ) collodion sections through an entire human breast give a closer approximation to the whole mount than thin sections taken from sample blocks of more convenient size.

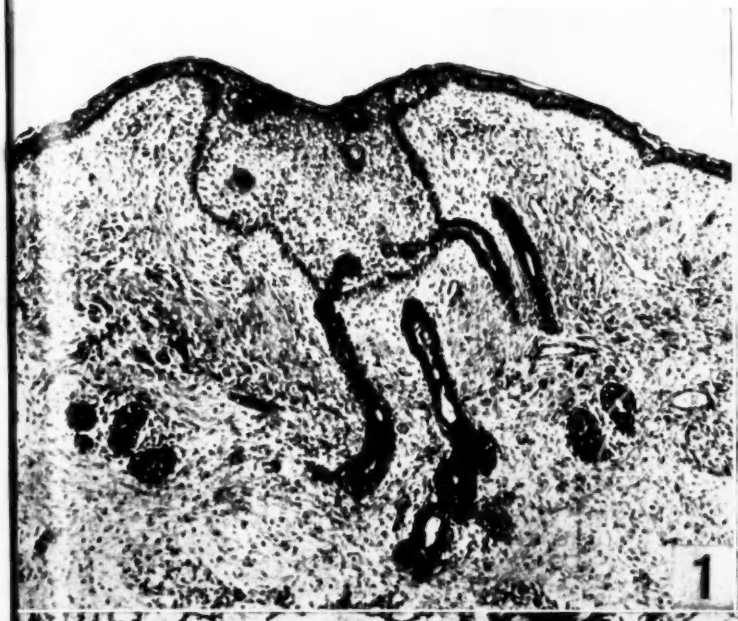
The pre-pubertal phase of the mammary gland in many species is characterized by a static, infantile condition consisting of primary ducts confined to the nipple-area. A very limited growth probably occurs in all forms in conformance with general body-growth. The female ferret and stoat exhibit an extreme degree of inactivity of the ducts, prolonged through the breeding season until pseudo-pregnancy or pregnancy. Amongst the important exceptions are the rat, mouse, calf, goat and monkey, in which the female mammary ducts undergo varying and often quite extensive development, which is usually accelerated in the period immediately preceding puberty. In the males of nearly all species the gland remains undeveloped, but in mice, rats and rabbits the ducts continue to proliferate between birth and puberty. Whatever degree of arborescence of the ducts occurs, it is generally agreed that no alveoli are formed during the pre-pubertal phase. Clearly it is important in researches, aiming at experimental development of the duct and alveolar systems, not to regard immature animals of a particular species as possessing inert mammary rudiments at the commencement of the experi-

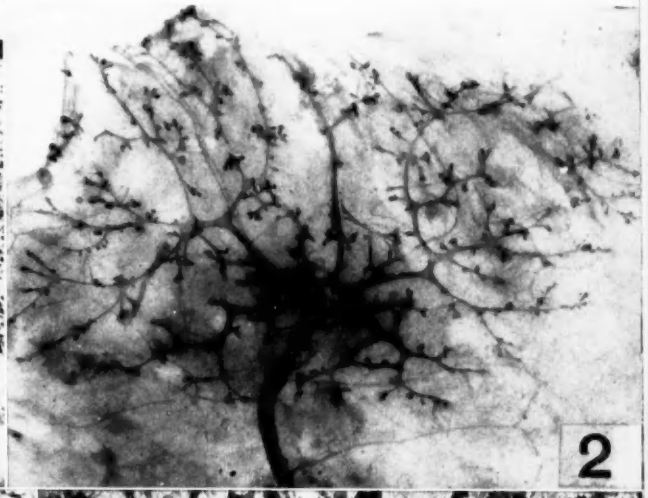
[1] [The secretion sometimes seen from the breasts of newborn infants.—Ed.]

MAMMARY GLANDS
IN VARIOUS STAGES OF DEVELOPMENT

(FIG. 1—8)

K. C. Richardson





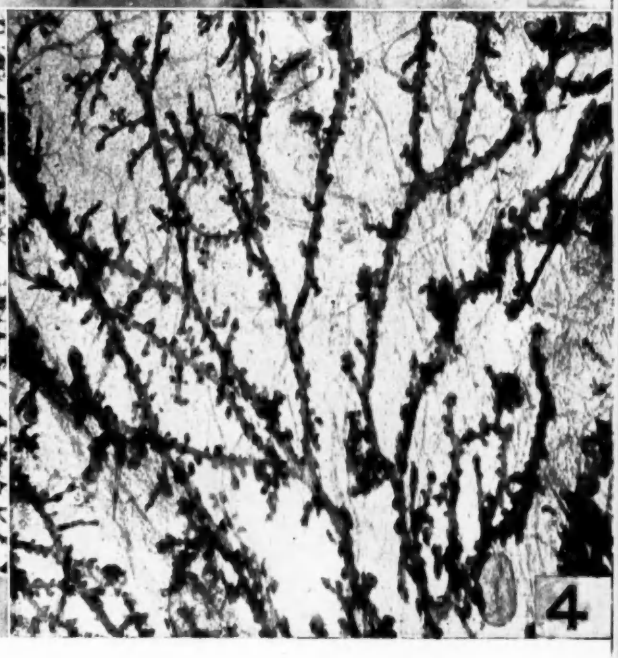


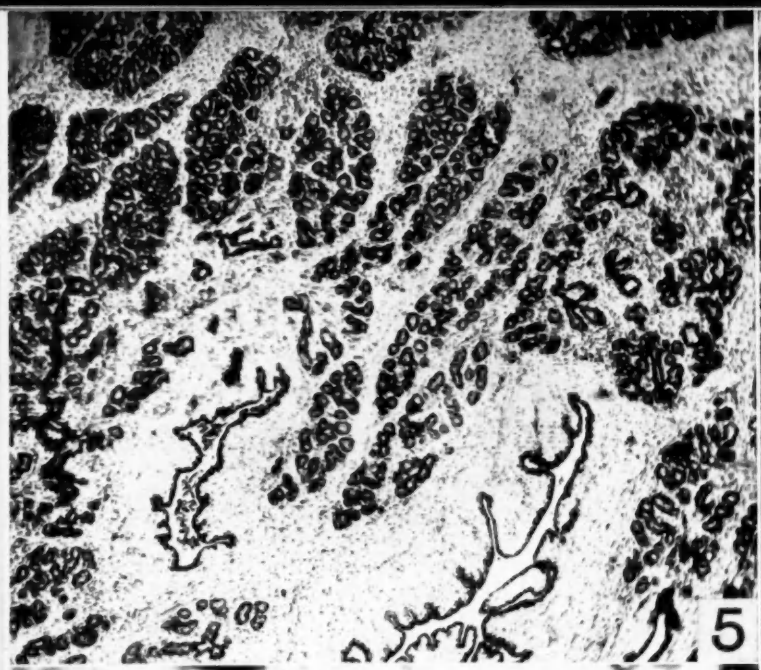
PLATE I
(FIG. 1—4)

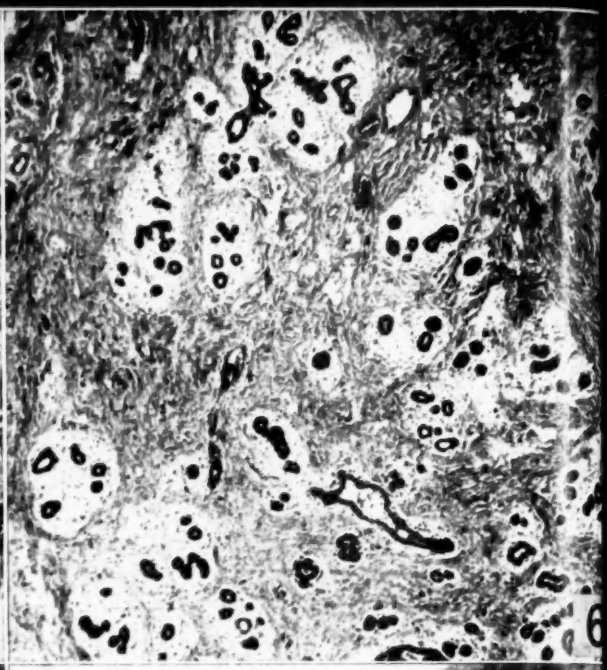
FIG. 1. Section of nipple-area (not yet elevated) from a male stillborn infant, showing the rudimentary ducts which are incompletely canalized (magnification ×85)

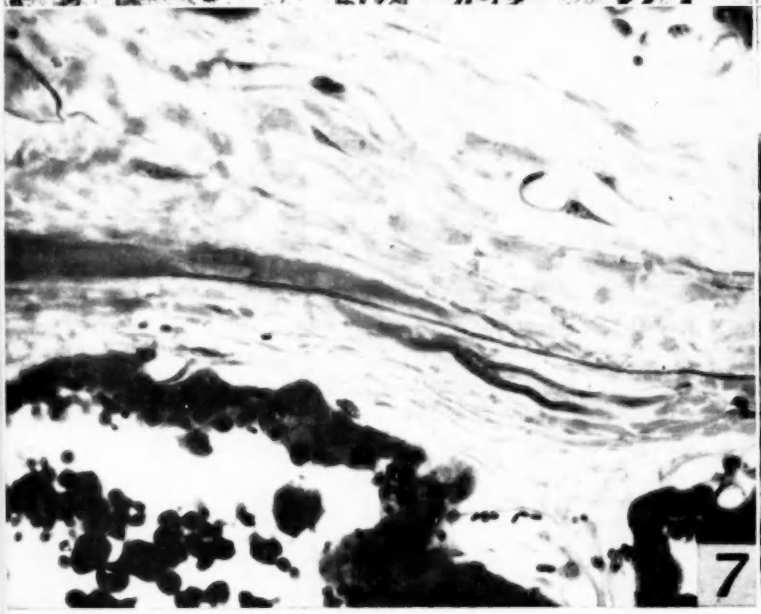
FIG. 2. Whole mount from a young female rhesus monkey approaching puberty (from the series described by Van Wagenen & Folley, 1939)

FIG. 3. Whole mount showing the greater part of a 1st thoracic gland from an adult female rat. (Preparation by A. T. Cowie.) (magnification ×5)

FIG. 4. The duct-system from the same gland as fig. 3, at higher magnification







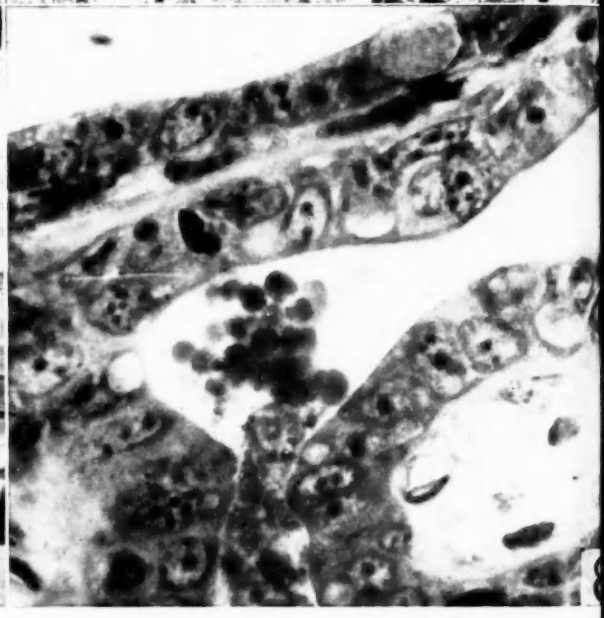


PLATE 2
(FIG. 5—8)

FIG. 5. Section showing growth during early pregnancy in a cat. The lobules are beginning to be outlined by the budding ducts and alveoli. Some large interlobular ducts are seen towards the centre (magnification ×64)

FIG. 6. Section from an adult human breast in the resting stage, illustrating the characteristic intralobular connective-tissue stroma immediately adjacent to the duct-tissue (magnification ×42)

FIG. 7. Smooth-muscle fibres, elastic fibres, collagen and blood-capillaries in the interlobular stroma of a goat-mamma

FIG. 8. Duct-epithelium in a lactating gland from a goat, showing secretory material in the duct-cells (magnification ×1500)

MAMMARY GLAND DURING LACTATION

(FIG. 9—15)

PLATE 3
(FIG. 9—12)

FIG. 9. Section of cat mammary gland in full lactation fixed by Hoerr's technique (1936), and stained with Heidenhain's haematoxylin. Numerous alveoli in lobules are distended with milk showing osmicated fat-droplets. Note the orientation of the fat towards the " upper " pole in most of the alveoli. This is a " creaming " effect which has taken place in the block of tissue before complete penetration of the fixative (magnification ×135)

FIG. 10. Alveoli from the same section as fig. 9. Note the grey, slightly granular protein coagulum and black fat droplets (magnification ×700)

FIG. 11. Lobules from the right half of a goat's udder, fixed by vascular perfusion with Helly's fluid, less than 1 hour after milking (see fig. 12). Note the shrunken alveoli with thick, folded epithelium, and the prominent interlobular septa (magnification ×80)

FIG. 12. Part of a lobule from the left, unmilked half of a goat's udder (see fig. 11) which was distended with milk and fixed by vascular perfusion. Note the dilated alveoli and ducts, and compare with the collapsed condition shown in fig. 11. The two photographs are at the same magnification

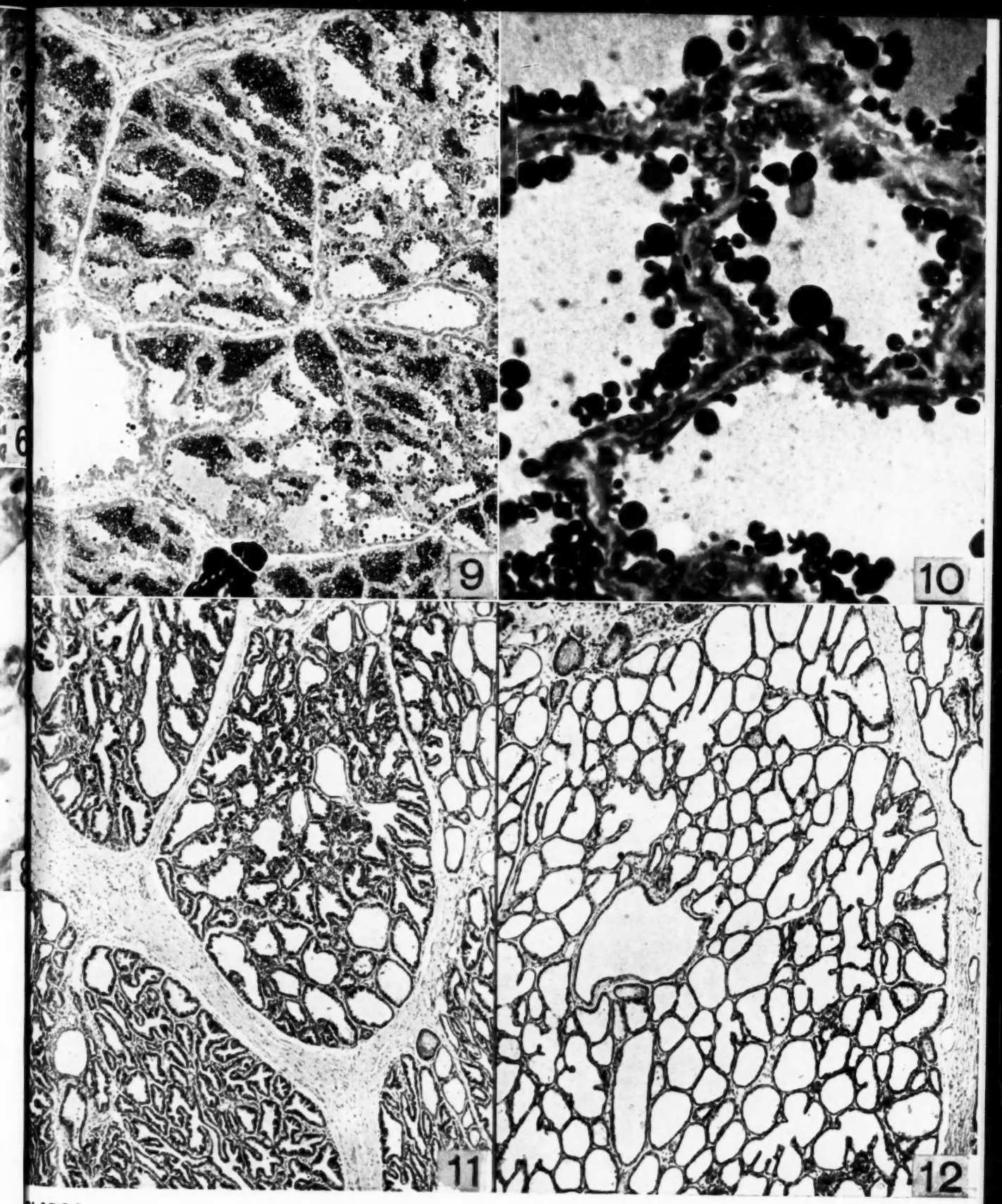
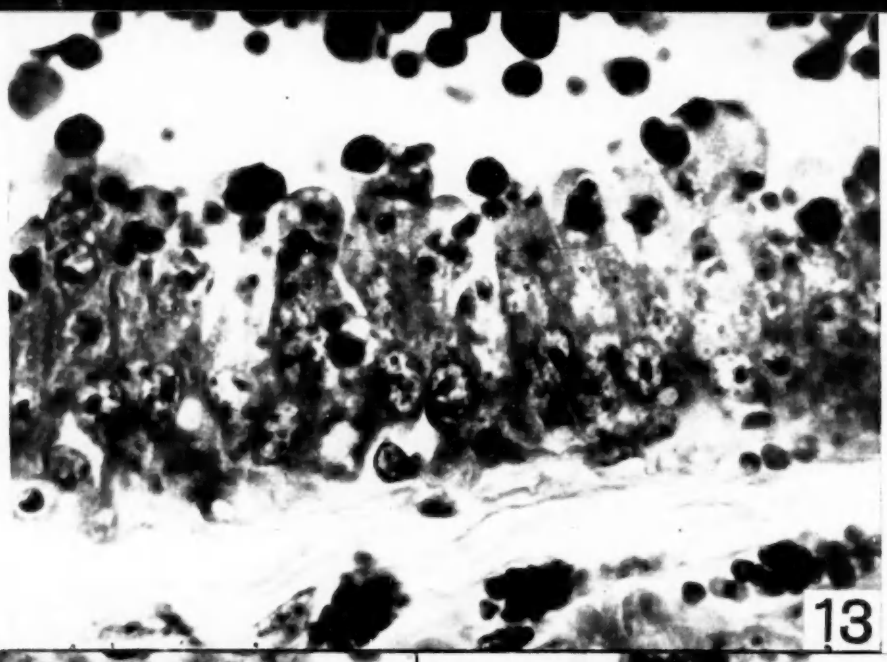


PLATE 3
(FIG. 9—12)



Photomicrographs by F. J. Pittock, F.R.P.S.

PLATE 4
(FIG. 13—15)

FIG. 13. Lactating epithelium from a goat in the early phase of secretion (Hoerr's technique). The cells are tall, and distended with dark-stained fat-droplets and -granules. Some of the fat is about to enter the lumen (magnification × 1500)

FIG. 14. Lactating epithelium from a goat, showing the terminal phase of the secretory cycle in a distended alveolus. Note the flattened epithelium (cf. fig. 13) (magnification × 1500)

FIG. 15. An intermediate stage of secretion (cf. fig. 13, 14) illustrating also the adjacent blood-capillaries (distended during fixation), the basement-membrane, and a nucleus marked "X" which appears to belong to a myo-epithelial cell lying between the epithelium and the basement-membrane (magnification × 1800)

ment without first checking the state of affairs in a given strain or species.

2. Development during Oestrous (menstrual) Cycles, Pseudopregnancy

So far we have traced mammary development in the form of epithelial tubes which are easily identified in whole mounts as a branching duct-system, the walls of which are composed of at least two layers of cells. In subsequent phases occurring during oestrous cycles, pseudo-pregnancy and pregnancy, further budding from the sides and terminal ends of the ducts now initiates in varying degrees the formation of lobules composed ultimately of numerous alveoli connected by intralobular ducts to the parent stems. It is a simple matter in many exocrine glands to distinguish precisely the location and limits of the alveolar cells from the epithelium of all the sub-divisions of the ducts. This is more difficult in the mammary gland, and it is questionable whether it can be done reliably in all species, while the gland is still immature, without careful examination of a large range of material taken in various phases. In following the growth of the mammary tree, the inexperienced observer may easily mistake the buds for the leaves. Sections can be most misleading because both the alveoli and the intralobular ducts are lined by a single layer of epithelium, all of it capable of secretory activity. This explains why there is often confusion in the earlier accounts of mammary development in various species as to whether the growth of true alveoli is attained in virgin animals. The prevailing generalization that oestrogens and progesterone stimulate respectively the growth of ducts and of alveoli is often taken rather too literally as indicating that a clear-cut distinction can be drawn between these two components of the gland during their early development.

With recurring oestrous cycles, as sexual maturity is attained, the virgin gland is stimulated for varying periods by oestrogen and progesterone. In most species it is possible to detect growth in the duct-system, the shape and numbers of the newly formed buds being characteristic of pro-oestrus and oestrus in some forms like the mouse. But the growth attained is soon lost by regression, only to be renewed again with the next cycle. A positive balance, so to speak, on the growth-side may result from failure of the ducts to regress completely after a period of stimulation. With the next cycle the mamma starts off somewhat ahead of the basal level of duct-tissue (fig. 3).

The prolonged luteal phase (pseudo-pregnancy), which is a natural feature of the cycle in such forms as the dog, fox and opossum, involves not only duct-growth, but a development of alveoli comparable with true pregnancy. Thus, the lactation occurring in some virgin bitches (Heape, 1906) is not a transient affair, and may be sufficient for the rearing of young. A further variation of some importance is found in those species in which a short or incomplete phase of pseudo-pregnancy can be induced experimentally by sterile copulation or cervical stimulation. In these cases mammary development extends as far as the alveolar growth typical of early pregnancy, but is then followed by regression when the luteal influence subsides.

In primates, successive menstrual cycles lead to the development of lobule-alveolar systems. Folley, Guthkelch & Zuckerman (1939) observed a gradual increase with age in the area of the mammary gland in nulliparous rhesus monkeys. The first cycles, which are usually anovulatory, were not accompanied by alveolar growth, but after ovulation alveolar tissue was identified. Speert (1941) has concluded from an extensive series of whole mounts of monkey glands that a definite series of cyclic growth changes occurs in fixed relation with the menstrual cycle.

For the human breast, Rosenburg (1922) claimed that premenstrual lobule-alveolar growth was followed by regression after menstruation. Others have denied that there is any clear correlation with the menstrual cycle. According to Dieckmann (1925) the growth, when it occurred, was more closely related to age, so that in some virgin women no lobules ever appeared, while in others lobules once developed were likely to be retained. In a recent account by Geschickter (1945), the histology of the female breast is discussed with reference to changes associated with the menstrual cycle. From an examination of more than 100 cases, of which the time of the cycle was definitely known, this author concludes that there is a proliferative phase of the duct-tissue, together with changes in the stroma, beginning a few days following cessation of menstrual flow. The growth extends through ovulation to reach a climax in the pre-menstruum. Variations frequently found within different lobules of the same breast, or related to hormonal irregularities in different individuals, were noted. Shortly before, or with the onset of menstruation, there is a regressive phase involving shrinkage or desquamation of the duct-epithelium. Thus the human breast seems to fall into line with what has been observed in the monkey. Finally we must add to the picture of conditions in the mature virgin mamma, the well-known anomaly that virgin goats of some pedigree stocks can be brought into lactation solely in response to the stimulus of milking. This species is remarkable for the duct-development exhibited at oestrus, but how far the glandular tissue is developed beyond this point, when the milking stimulus is applied, requires further investigation.

3. Development during Pregnancy

The growth-changes during pregnancy will depend on how far the ducts have developed in the virgin animal before fertilization, or to what extent involution has reduced the duct-system after the last pregnancy and lactation. With few exceptions, according to Turner (1939), the first half of pregnancy is occupied by the development of ducts, lobules and alveoli (fig. 5). The last units are in the form of clusters of glandular cells with a small lumen which becomes slowly distended as the secretion is formed. During the second half of pregnancy, secretory activity becomes more and more prominent, increasing the general size of the mamma because the alveoli and ducts are dilated. Some species begin with almost a minimum of duct-tissue, and pass through an extensive phase of budding before lobules and alveoli appear. In these cases (e.g. dog) it probably takes more like two-thirds of the period of pregnancy before cellular proliferation wanes. The cow is remarkable in requiring very little duct-growth to establish the full extent of its lobules. In the goat, secretory activity is unusually late in appearing, so that there is a phase of rapid enlargement of the alveoli at approximately 100 days. The impression gained from a rather limited range of human breasts removed in early pregnancy, is that approximately 5 months are required for lobule-alveolar development

and the commencement of active secretion. The budding of alveoli was observed by Dawson (1935) to begin at about the 10th week, when increase of glandular tissue becomes noticeable clinically.

From the experimental point of view, perhaps the most important feature of structural development during pregnancy in human and other animals is that lobules of individual glands, or even more extensive areas, may fail to reach maturity. Engel (1941) points out that there is wide variation in the architecture of the lactating breast in women and animals which may be missed in sections from areas selected at random. He stresses the value of thick sections of entire breasts in assessing these variations. In the human hypogalactic breast, the glandular tissue in the central region and main body of the gland may be negligible.

4. The Lactating Gland

The structural investigation of mature alveoli in late pregnancy and during lactation (fig. 9, 10) has been pursued repeatedly since about the middle of the last century. There are few examples in the histology and cytology of glandular tissues where so much disagreement has occurred concerning the main outlines of cell-behaviour during the secretory cycle. The finer analysis of cytoplasmic and nuclear changes associated with secretion has been a controversial field in all glands, but in the mammary gland it is the gross structural changes of which we are still uncertain. The problem is of course largely a technical one. The lactating gland is like a sponge soaked in milk. Cutting prior to fixation involves squeezing it, with shifting and extrusion of the stored secretion. When this secretion accumulates in large amounts, it causes the alveoli and ducts to distend (fig. 12, 11). A high milk-pressure, suddenly released by cutting the living gland, will be followed by elastic recoil of the stroma, and distortion of the alveoli. It is curious how few histologists have used material fixed by intravascular perfusion and hardened *in toto*, before isolating the usual small sample blocks for imbedding. So little information is usually given in histological and cytological papers on the lactating gland, as to its state of distension, or whether the material has been taken after a period of rest, or immediately following suckling or milking. The more detailed work has been done largely on rodent glands in which it is difficult to estimate or control these factors. These rather obvious, but often neglected, details of technique have been mentioned, firstly because they are relevant to the interpretation of the normal alveolar secretory cycle, and secondly, as will be shown later, because quantitative estimation of the development of functional alveoli must take into account their state of distension.

It is generally agreed that the alveolar epithelial cell undergoes considerable change in shape, partly at least in response to the distending effect of accumulating secretion, or the collapse which follows its removal. The entire lobule, as well as the alveoli, shrinks when the gland is emptied (fig. 11). If we take the empty stage as the starting-point of a secretory cycle, we find that the alveolar epithelium is often folded, and its cells are so elongated that the apical cytoplasm projects in an irregular fashion into the empty lumen. Soon after the removal of milk from the alveoli, the secretory antecedents accumulate again in the cytoplasm in the form of fat-droplets of relatively large size (fig. 13), together with less-conspicuous granular protein. As more and more milk is secreted into the alveolar lumen, the cells become stretched, often to a very thin layer (fig. 14, 15). It is the mode of release of the secretory material from the cells which has been so much debated. There are three possible ways in which the secretion may leave the cells to enter the lumen :—the protein, fats and soluble components may pass through an intact cell-membrane ; the membrane may be ruptured irregularly to release the larger secretory masses, particularly the fats ; or the apical cytoplasm may become detached (pinched off or decapitated), leaving the cell to undergo a rapid phase of regeneration.

It is often forgotten that the same materials are released from the alveolar cells during the secretory phase of pregnancy, though in different concentrations, and at a slower rate. Grynfeltt (1937a) has investigated the cell-changes in the alveolar and duct epithelium during pregnancy. He points out that a basal secretion of protein granules is transported from the cells to the lumen without obvious breakdown of the cytoplasm or cell-membrane. Large fat-droplets, appearing sporadically in less concentration than in the lactating gland, are also extruded without causing the " ragged " surface so characteristic of the lactation-phase. Is the so-called apocrine type of secretion a consequence of the more rapid rate of secretion in the lactating gland ; an effect of suckling ; or an insignificant process on the part of some over-active cells exaggerated by technical manipulation ? Unfortunately conditions are unsuitable for direct observation of living alveoli, as can be done with glands like the intact pancreas. It is probable that in any case the fat-droplets would hinder resolution sufficiently to make the method unreliable.

We must be content to follow the opinions of authors who have re-examined the problem of alveolar-cell behaviour in recent years. Jeffers (1935) describes a cell-cycle, for instance, in the rat which involves a decapitation of the apical cytoplasm during the early stages of secretion when the cell is still elongated. In collapsed alveoli, however, when a fresh cycle of milk-secretion is beginning, it is common to find the epithelial cells cut in various oblique planes. Thus " decapitation " may result from the section-cutting. Unless some form of reconstruction is attempted from serial sections, the apparently isolated patches of cytoplasm containing secretion, which have been so often described in the lactating alveolus, should be interpreted with caution. This is especially so when the material has already been disturbed by attempting to cut it into small fragments for so-called cytological fixation. On the other hand the extrusion of large fat-droplets from the cytoplasm does appear to result in a rupture of the cell-membrane, if we are to interpret the ragged appearance of the fixed and stained lactating epithelium as not due entirely to a technical artifact following extraction of fat. Grynfeltt (1937b), however, distinguishes two types of fat-secretion. He interprets the ruptured appearance of the cell-membrane as brought about by rapid withdrawal of the secretion during suckling. Cells which are not injured in this mechanical way appeared to him to release their fat more gradually, without obvious destruction of the cell-membrane. The effects of suckling were, however, surmised rather than investigated under controlled conditions. Even this effect of a ruptured membrane may be due to, or exaggerated by, inadequate technique during fixation and imbedding. It is

useless to argue further on these points until more is known of the factors controlling the secretion of fat and protein in the milk. If it were possible by some experimental means to suppress or augment the secretion of one or other component independently, we might get further information to settle the controversy. It is fair to say that the apocrine mode of secretion has probably been much over-emphasized, if it occurs at all.

Our interest in the structural behaviour of the alveolar epithelium is concerned, however, with more than the mere academic problem as to whether the mammary glands fit into the apocrine group. We must know the details of the secretory cycle, for instance, to account for variations in the composition of milk. Do all the epithelial cells of an alveolus undergo the different stages of the secretory cycle in unison, or at random? If wholesale decapitation of alveolar cells is the rule in secretion, what is the rate of regeneration, and how long is the interval before a new cycle of secretion is possible?

Turner (1935) has put forward a theory of milk-secretion for the domestic animal which, whether right or wrong, serves to illustrate how the structural behaviour of the alveolar cells may be significant in explaining variations in milk-composition. This theory depends on the assumption that the intra-alveolar pressure resulting from accumulation of milk slows down the rate of secretion, possibly owing to pressure on the capillary blood-vessels. If the interval between milkings is sufficient for regeneration of the cell-membrane, ruptured previously during the active phases of secretion or withdrawal, the alveolus in its distended state will reach a stage when fat-droplets are unable to pass freely through the re-constituted cell-membrane, although other components of milk may continue to do so at a retarded rate. There may be a relationship, in other words, between alveolar pressure and slowing of secretion, with a selective inhibition of the release of fat. When the milk-pressure is low, the fat-content will be high; but as the interval between milkings is extended, the fat-content of the total yield will be reduced by dilution of the milk with water and substances which can pass freely through an intact membrane.

5. Involution

Involution of the mamma begins rapidly following failure to withdraw the secretion. The structural changes involved in the reduction of a fully-developed gland to a resting-condition roughly comparable with that in the virgin animal have not been investigated in quite the same detail as those associated with the reverse processes of growth and lactation. The main outlines are, however, well known. From detailed study of involution in the mouse, Williams (1942) has shown that the regression is more rapid if the young are removed at birth, before suckling can begin, than if weaning occurs during the height of lactation. There is a temporary phase of secretory engorgement, during which the protein coagulum in sections becomes more intensely staining, followed by absorption of the milk and collapse of the alveoli. The epithelium appears to disintegrate in various ways by vacuolation and pycnosis, frequently forming coalesced masses of cells when the alveolar pattern is destroyed. In the domestic animals, which are milked regularly, the involution is more gradual, spreading slowly through the gland and reducing the active tissue unevenly (see Lenfers, 1907). According to McFarland (1922), involution rarely proceeds uniformly in the human breast. A few lobules may remain for one year following birth, and vestiges of lobules may be found even in advanced age.

6. Some Abnormal Variations of Growth and Differentiation

It is not proposed to carry this account into the extensive field of mammary pathology, but it should be stressed that, as a result of experimental work on the hormonal factors controlling mammary development and lactation, some at least of the well-known pathological changes observed in the human breast have been induced in identical or closely-similar form in animals. Mammary epithelium is so sensitive to the action of hormones that the pattern of its growth, and indeed the structural differentiation of its cells, may become abnormal. Apparent over-stimulation, following excessive dosage with one kind of hormone, or failure to give correctly-proportioned dosages where two or more hormones are concerned, may result in effects of this kind. For optimum growth of the duct-system, for instance, it seems clear that the oestrogen-dosage must be kept within fairly narrow limits. High dosages result in the mouse and monkey, as Gardner, Smith & Strong (1935) and Gardner (1941) have shown, in the development of stunted glands (see Folley, 1947a). From such abnormally developed duct-tissue, cystic dilations may arise. The mammary alveolus also can grow abnormally, even although normal milk-secretion is ultimately attained. Thus, Mixner & Turner (1943) found abnormally enlarged alveoli with characteristic proliferations of the epithelium developing in virgin goats brought into lactation by the administration of oestrogen. Structurally, these abnormal alveoli appear to be similar to the cystic alveoli of the human breast, regarded by McFarland (1922) and others as residual lactation-alveoli, which had failed to involute, and had become dilated by persisting secretion. Even the epithelial folding is identical, being due in all probability to the disruption of inter-alveolar septa rather than a papillomatous proliferation. The human condition may in fact be a feature of atypical growth occurring before lactation, rather than an abnormal persistence of alveoli following involution. Turning to the mammary epithelial cell itself, we find a possible link between the pale or "pink" granular epithelium commonly found in cystic disease of the breast (see Lendrum, 1945) and a similar cellular change described by Speert (1942) in monkeys, after prolonged oestrogen treatment. If these two variants of mammary epithelium are identical, the experimental material would seem to show that the change begins during the growth-phase before the alveoli mature, probably at a time long before cystic enlargement is established.

7. Quantitative Estimation of Mammary Growth

Both in the fields of normal development and of pathology, the qualitative description of growth and differentiation in mammary tissues should be supplemented where possible by more experimental work involving quantitative measurement. Gardner & Strong (1935), Van Heuverswyn, Folley & Gardner (1939), Folley *et al.* (1939), and Dubois (1944), are amongst the few authors who have attempted to express mammary growth in semi-quantitative form. The last two papers quoted above deal with surface-area

measurements obtained from whole mounts. But growth occurs also by densification of the mammary tree, due to budding of vast numbers of off-shoots eventually terminating in alveoli (fig. 4). Cowie & Folley (submitted for publication) have devised a system of scoring from whole mounts in rats by which each kind and degree of mammary development may be assessed. All the glands from individual rats were estimated with regard to arborescence of the duct-system, the presence of club-shaped end-buds, side-buds, and alveolar development. The slides from all rats of one sex (in a particular experiment) were randomized, and scored by the two authors independently. The score was then subjected to an analysis of variance.

The problem of measuring the development of a fully lactating gland, for instance in large domestic animals, is rather more difficult. The data relating to milk-yield have usually been given in combination with a qualitative appraisal of the development of the gland as seen in small sample blocks taken at random. What is required in experiments involving, for instance, the artificial growth of a lactating udder in a virgin animal, is some more accurate method of estimating the amount of functional alveolar tissue, and the proportion which is incompletely or abnormally developed, together with some volumetric measurement of the gland- and teat-cisterns. It is suggested that fixation of the udder by vascular perfusion, when it is in a state of full distension with stored milk, followed by preparation of thick (100 μ) collodion sections, will assist in providing this information. It is most desirable with experimental material of this kind to be able to relate the performance of a gland with quantitative measurements such as the average size of alveoli, and the total amounts of glandular tissue and stroma.

8. Connective-tissue Stroma of the Mammary Gland

How far the varying textures and growth-behaviour of the connective-tissue stroma of the mammary area may influence the extent of arborization of a growing gland is at present unknown. There are marked variations in the proportions of fibres, cells, and intercellular matrix in this stroma, and these are particularly evident in the human breast (fig. 6) and the udders of domestic animals. It is fairly certain that the development of adipose tissue in the form of lobules mimics to some extent the lobular growth of the gland. Turner (1931) emphasizes the importance of the fatty pad or cushion, present in the udder of the foetal female calf, responsible until pregnancy for the greater part of its volume. This pad is absent in the male goat (Turner, 1936), as well as the steer, which may account, partly at least, for the failure of Folley, Scott Watson & Bottomley (1941), and Folley & Malpress (1945, unpublished observations) to induce normal udder-development by hormonal treatment in the males of these two species.

When the duct-tissue has ramified sufficiently through the stroma to establish the pattern of future lobules, it is well known that the connective tissue immediately adjacent to the ducts becomes more cellular and less fibrous than the interlobular areas (fig. 6). There is an increase in the intercellular matrix, often described as a mucinoid change. Somewhat similar, though not identical, changes in connective tissue have been described in other regions of the body influenced by sex hormones. Thus the erection of the cock's comb, so dependent on male hormone, is associated with a deposition of mucoprotein in the intercellular spaces (see Hardesty, 1931). Aykroyd & Zuckerman (1938) found that the swelling of the sexual skin in monkeys, following oestrogen stimulation, was due to a transference of water, supplemented by increases in mucoprotein, which they ascribed to the discharge of granules from connective-tissue mast-cells. A remarkably localized transformation of connective tissue in response to sex-hormone administration is described by Heringa & de Jongh (1934) as occurring around the ampulla of the vas deferens in castrated mice treated daily with oestrogen. In this case, the connective tissue underwent a mucoid change closely resembling that in the intralobular areas of the mammary gland.

9. Mechanism of Expulsion of Milk

Finally, we must turn our attention to the general problem as to how milk is expelled from a lactating gland. The mere mechanical effect of suckling, or the manipulation of the teat and udder in milking, will not remove all the milk stored in the alveoli and ducts. Capillary attraction in the finer ducts and alveoli restricts the movement of the secretion and, when suction is applied, there is a resistance to withdrawal of milk owing to a valve-like collapse of the larger ducts. Some contractile force, closely associated with the alveoli, appears to be necessary to shift the milk towards the larger ducts or cisterns. It is a mechanism of this kind which is prominent in the phenomenon of "let-down" so well-known in bovines. The forcible extrusion of milk which follows the injection of posterior-pituitary extracts reveals a powerful response of some kind of contractile tissue.

In the salivary glands, which have been investigated with greater precision, it is possible to distinguish several factors influencing the expulsion of the secretion :—secretory nerves ending directly on the glandular cells, alterations in blood-flow, and internal pressure-changes which seem to take origin in some contractile tissue like smooth muscle. Babkin (1944) discusses how each separate mechanism has been examined experimentally in animals. The less-complex mammary gland does not appear to possess secretory nerves directly affecting the rate of synthesis and discharge of the milk-components from its cells. We are left with the possible alternatives that either an erectile effect is produced by vascular engorgement, which squeezes the glandular tissues, or that some contractile tissue exists which on the one hand compresses the alveoli, and on the other shortens the ducts and keeps them open. As the available experimental evidence (see Folley 1947b)[3] favours the second alternative we must examine the distribution of contractile tissues in the mammary stroma.

Smooth muscle is easily identified in all forms in association with the teat or nipple, where circular fibres act as sphincters, and longitudinal or oblique fibres appear to assist in dilating the ducts. Similar but less-regular muscular bundles extend through the walls of the gland-cistern, if present, and then gradually the smooth-muscle fibres decrease as they are traced along the principal branches of the duct-system. Scattered smooth muscle is mingled with the connective tissue and vessels of the interlobular septa in some forms (fig. 7). A closer relationship between

the alveoli and true smooth muscle is seldom found. Thus, the impression is gained that the distribution of smooth muscle subserves an effective control of the duct-system, but it is unlikely to account for contraction of alveoli, if this really occurs.

In a classical paper on the relations of the mammary- and sweat-glands, Benda (1894) described the existence of flattened (myo-epithelial) cells lying between the epithelium and basement-membranes of both these glands. He considered these cells to be contractile in function. Cells, similar in origin and presumably in function, were described in the salivary glands, where they are often called basket-cells, being star-shaped with processes which envelop the external surface of the acini. Unfortunately, these cells are difficult to stain completely and selectively. Their innervation, if any, is obscure. They appear to be numerous around the larger mammary ducts, and have been observed by Kuzma (1943) to undergo hyperplasia in the human breast. Whether they are present immediately outside the alveolar epithelium in all species is still open to doubt. Dieckmann (1925) and Hammond (1927) have contended that the cells, identified by other authors as myo-epithelium in the mammary gland, are in fact adventitial cells belonging to the closely adjacent blood-capillaries.

A further attempt to affirm the existence of these cells in mammary alveoli has been made more recently by Swanson & Turner (1941). Histologists familiar with the work of Zimmerman (1927) and with the photomicrograph of a salivary basket-cell illustrated by Babkin (1944) may have some hesitation in accepting the evidence given by Swanson & Turner, especially as these authors use the term smooth muscle to cover cells in contact with the epithelium, as well as those mingled with the connective tissue of the stroma. It would be pedantic to stress the independence of these cells, were it not that the evidence for contractility in myo-epithelium is so slender.

Babkin (1944) has assembled experimental evidence from various sources which seems to indicate that the contractile tissue in salivary glands is unlike smooth muscle in its pharmacological responses. Although vasodilation, with sudden filling of the capillary vessels, might conceivably press out the saliva from the acini, the "expressor" effect of histamine, for instance, cannot be correlated sufficiently clearly with its dilating effect on the blood-vessels. By a process of elimination, Babkin comes to the conclusion that the only contractile cells remaining in salivary glands, whose activity might be involved in such phenomena as augmented sympathetic-after-chorda secretion, are the myo-epithelial or basket-cells. May we end by quoting Babkin's own words? "Unfortunately there is no direct evidence of their ability to contract. Further investigation of this problem is very desirable, and will afford an excellent opportunity for co-operation between physiologists and histologists."

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ENDOCRINE CONTROL OF THE MAMMARY GLAND

I. Mammary Development

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1 Ovarian hormones
2 Anterior pituitary
3 Adrenal cortex
4 Placenta
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The outstanding fact regarding the nature of the factors immediately controlling mammary development became apparent many years ago. This was the recognition that mammary growth is under the control of hormonal rather than nervous stimuli. Transplantation-experiments, of which a comparatively modern example is that of Stricker (1929), were perhaps the most decisive in establishing this conception. For an account of early work in this field, and of the normal development of the mammary gland, the reader is referred to Turner (1932) and Turner (1939a) respectively.

An important point which has emerged from morphological studies of mammary development during pregnancy is the necessity to distinguish between the growth-phase, which appears to be largely confined to the first half of pregnancy and the secretory phase beginning at mid-pregnancy, which is accompanied by an increase in the size of the mammary gland due, not so much to further growth, as to accumulation of secretion in the glandular tissues. This conception has recently been confirmed by a biochemical study (Folley & Greenbaum, 1947) in which it was shown, by estimation of the milk-content of the rat mammary gland, that the true moist weight of tissue remains sensibly constant from mid-pregnancy until the end of lactation.

1. Ovarian Hormones

Earlier work on the endocrine control of mammary development has been reviewed by Nelson (1936), Turner (1939b) and Folley (1940). Readers should consult these articles for further information since only the briefest references to any but modern work will, in general, be possible here. The broad conclusion emerging from this considerable body of work was that while full duct-development could be evoked by treatment with oestrogen alone, such treatment in many species was incapable of causing development of a normal lobule-alveolar system. For full alveolar development, combined treatment with oestrogen and progesterone was necessary in many species. Nevertheless, species differences in the mammary response to oestrogen alone have become apparent, and in some cases there is evidence that oestrogen alone can develop both duct and alveolar systems. Notably in the guinea-pig, it was soon apparent that very considerable, if not complete, mammary development could be experimentally induced by oestrogen alone, and more recently it has become clear that the same applies to the goat, cow, and perhaps the monkey.

In the goat, experimental development of an udder capable of secreting considerable quantities of milk has been achieved by treatment with oestradiol monobenzoate (de Fremery, 1938) and with synthetic oestrogens (Folley, Scott Watson & Bottomley, 1940, 1941; Lewis & Turner, 1940, 1941, 1942a; Mixner & Turner, 1943; Mixner, Meites & Turner, 1944; Folley, Malpress & Young, 1945). Even more striking results in bovines have been reported by Walker & Stanley (1940, 1941), Reece (1943), Folley & Malpress (1944a, 1944b), Folley, Stewart & Young (1944), Hammond & Day (1944), Parkes & Glover (1944), Day & Hammond (1945), Folley *et al.* (1945), and Spriggs (1945). The abundant yields of milk produced by the treated animals could have been produced only by well-developed lobule-alveolar systems and, though intact animals were used in most of the experiments, positive responses with a spayed heifer (Walker & Stanley, 1940, 1941) and a freemartin (Folley & Malpress, 1944a) testify to the non-essentiality of luteal influence. Mixner & Turner (1943), however, report that, in the goat, oestrogen alone resulted in the development of abnormally large alveoli often characterized by papillomatous outgrowths of the epithelium into the lumen; combined treatment with oestrogen and progesterone gave a more normal histological picture. The hormonal induction of mammary growth in ruminants is considered further in an accompanying article[1] by Malpress (1947).

In the monkey also, oestrogen seems capable of causing alveolar development as well as duct-development, particularly in the female (Gardner & Van Wagenen, 1938; Folley, Guthkelch & Zuckerman, 1939; Gardner, 1941a). Strikingly positive results on a few males (Gardner & Van Wagenen, 1938; Gardner, 1941a) may or may not be significant, since Folley *et al.* (1939) observed gynaecomastia in one of five normal male monkeys.

In considering the significance of such results as those just discussed in respect of the guinea-pig, ruminant and monkey, it must be remembered that progesterone has been isolated from the adrenal cortex (Beall & Reichstein, 1938), so that the possible intervention of extra-ovarian progesterone in experiments carried out with oestrogen alone on males or ovariectomized females has never been wholly excluded.

An interesting point regarding stimulation of mammary growth by oestrogen is the discovery that for optimal development of the duct-system the dosage of oestrogen must be maintained within circumscribed limits. Gardner, Smith & Strong (1935) first reported that in the mouse stunted duct-systems are the consequence of stimulation with excessive oestrogen levels. This finding has since been confirmed in the mouse (Gardner, Smith, Allen & Strong, 1936; Van Heuverswyn, Folley & Gardner, 1939;

[1] [*BMB* 1105]

and Gardner, 1941a), rat (Astwood, Geschickter & Rausch, 1937), rabbit (Scharf & Lyons, 1941) and monkey (Gardner, 1941a).

It was once believed that progesterone alone was incapable of stimulating mammary growth; that it would evoke alveolar development only in combination with oestrogen, or at any rate, in glands which had previously come under the influence of oestrogen. Gardner & Hill (1936) showed this to be a misconception, when they found that high doses of progesterone would stimulate mammary development in mice not previously or simultaneously treated with oestrogen. Confirmation has since followed in the mouse (Mixner & Turner, 1942a, 1943; Chamorro, 1944), rat (Selye, 1940a, 1940b; Reece & Bivins, 1942; Selye, Borduas & Masson, 1942; Chamorro, 1944), and monkey (Hartman & Speert, 1941). Relatively large doses must be used—of the order of 15 mg. daily in the rat.

From these studies and others, such as those of Scharf & Lyons (1941) and Lyons & McGinty (1941) in the rabbit, and Mixner & Turner (1942a, 1943) in the mouse, in which optimal oestrogen/progesterone ratios for lobule-alveolar development were determined, it is clear, if one adopts the view that progesterone is the primary agent responsible for lobule-alveolar growth, that much less is required in the presence of oestrogen than in its absence. Mixner & Turner (1943) have advanced a theory which, if it is valid, permits an explanation of this apparent "progesterone-sparing" action of oestrogen. They believe that oestrogen causes an increased vascularity and hyperaemia in the mammary stroma associated with a heightened vascular permeability, all of which factors would favour access to the gland tissues of mammary-stimulating hormones (in point of fact, as will be seen in the next section, believed by Mixner & Turner to be special anterior-lobe hormones) and metabolites specially needed by growing tissues.

2. Anterior Pituitary

Though certain workers (Corner, 1930; Lyons & Catchpole, 1933) had previously drawn attention to the possibility that the anterior pituitary might be concerned in mammary development, by virtue of claims to have demonstrated mammary growth in response to anterior-pituitary extracts, this idea assumed prominence only when certain workers failed experimentally to stimulate mammary growth in completely hypophysectomized animals by stimuli which would have been expected to be effective had the pituitary been present. Oestrogen alone or combined with progesterone was found to be ineffective in stimulating mammary growth in completely hypophysectomized mice (Gomez, Turner, Gardner & Hill, 1937; Gomez & Turner, 1937; Lacassagne & Chamorro, 1939), rats (Reece, Turner & Hill, 1936; Astwood *et al.* 1937; Gomez & Turner, 1937; Nathanson, Shaw & Franseen, 1939; Reece & Leonard, 1941; Samuels, Reinecke & Petersen, 1941; Leonard & Reece, 1942; Reece & Leathem, 1945) and guinea-pigs (Gomez & Turner, 1936, 1937; Lyons & Pencharz, 1936). Turner and his school were thus led to put forward the "mammogen" theory, according to which oestrogens were held to stimulate mammary-duct growth not directly, but indirectly by evoking the secretion by the anterior pituitary of a duct-growth-stimulating hormone, later known as Mammogen I.

In support of this theory, it was shown that mammary growth could be induced in hypophysectomized male guinea-pigs by daily implants of pituitaries from oestrogen-treated rats, but not from untreated controls (Gomez & Turner, 1937; Gomez, Turner & Reece, 1937), and that while mammary-growth-stimulating (mammogenic) activity was exhibited by extracts of anterior pituitaries from pregnant cows, which should be actively secreting the mammogenic hormone or hormones, extracts made from pituitaries of non-pregnant cattle were ineffective (Gomez & Turner, 1938).

The postulation of the existence of two mammogenic hormones, Mammogen I, responsible for evoking growth of the mammary-duct system and secreted by the anterior pituitary under the influence of oestrogen, and Mammogen II, which causes lobule-alveolar growth and is secreted by the anterior lobe in response to stimulation by progesterone, represented the final development of the mammogen theory (Lewis & Turner, 1939; Mixner, Lewis & Turner, 1940). Further studies on the second mammogenic hormone were reported by Mixner & Turner (1943), who describe a method for its assay, using spayed female mice also receiving oestrogen.

Until quite recently, the mammogen hypothesis was characterized by a rather surprising feature, namely, the belief (Lewis & Turner, 1938, 1939; Gomez, 1942; Lewis, Gomez & Turner, 1942) that Mammogen I was, unlike the well-characterized anterior-pituitary hormones which all appear to be proteins, soluble in organic solvents. Greep & Stavely (1941) were, however, unable to confirm this claim, which has since been withdrawn (Trentin, Lewis, Bergman & Turner, 1943). This Missouri group now finds that mammogenic activity resides in the protein fraction.

In any assessment of the present status of this interesting hypothesis, a number of discordant results must be taken into account. In the first place, positive mammary-growth responses to various steroids in completely hypophysectomized animals have been reported (Asdell, Brooks, Salisbury & Seidenstein, 1936; Fredrikson, 1939; Gardner, 1940, 1941b; Gardner & White, 1942; Leonard, 1943; Smithcors & Leonard, 1943), though in most cases the amount of growth was limited. Further, some authors (Nelson, 1938, 1939; Reece & Leonard, 1939) have been unable to confirm the claim that pituitaries from oestrogenized donors contain more mammogen than those from controls.

Perhaps the most serious objection may be based on the results of experiments in which it was found that percutaneous application of minimal, or near-minimal, doses of oestrogen to one rudimentary mammary gland will cause development of the treated rudiment, while neighbouring glands show either no effect or grow to a much smaller degree (see MacBryde, 1939, for woman; Lyons & Sako, 1940, rabbit; Nelson, 1941a, guinea-pig; Gardner & Chamberlin, 1941, mouse; Speert, 1940a, and Chamberlin, Gardner & Allen, 1941, monkey). These results, which should not be confused, as Petersen (1944) seems to have done, with generalized mammary development in ruminants (Folley *et al.* 1940, 1941) evoked by inunction of the perithelial skin with doses of oestrogen probably sufficient to cause systemic effects, at first sight would appear to provide conclusive evidence of the direct action of sex hormones on the mammary gland, since if

this action were indirect via the anterior pituitary, the action would in fact be systemic, resulting in equal growth in all glands. Mixner & Turner (1943) have, however, attempted an ingenious explanation of these findings in terms of the mammogen theory. They suggest that the action of the percutaneously-applied oestrogen causes localized hyperaemia of the mammary stroma, resulting in an increased and effective supply of mammogenic hormones already circulating in sub-threshold concentration. However, attempts to evoke localized mammary growth by percutaneous application of a rubefacient such as turpentine, alone or combined with oestrogen given systemically (Mixner & Turner, 1941 ; Lewis & Turner, 1942b), hardly afforded convincing support for this explanation.

The foregoing discussion, necessarily condensed but, it is hoped, adequately covering the main points, reveals a rather confused situation regarding the role of the anterior pituitary in mammary development. Further work is clearly needed to clarify this picture. The experiments on localized mammary growth and the results of those workers who have demonstrated even slight mammary-growth responses to steroids in completely hypophysectomized animals together make a case for the direct action of ovarian hormones on the mammary tissues which, in the writer's opinion, has not yet been overturned. That the co-operation of the anterior pituitary (or of some other organ such as the placenta which, as will be seen in a following section, may be capable of substituting for some function of the anterior pituitary) may be necessary for the full expression of this action is indicated by the experiments of Leonard & Reece (1942), who could not obtain localized mammary responses to oestrogen in hypophysectomized animals, and by the fact that in the experiments in which mammary growth has been evoked by systemic injection of steroids the responses have usually been slight. This, however, does not affect the point at issue.

On the other hand, few would deny the validity of the evidence which suggests that crude anterior-pituitary extracts contain factors capable of promoting mammary growth in gonadectomized and even hypophysectomized animals. In addition to the Missouri group, other workers (*e.g.* Greep & Stavely, 1941 and Cowie & Folley, 1944, 1947) have found that anterior-pituitary extracts will promote mammary growth in gonadectomized animals. The point of uncertainty is whether these effects are due to new anterior-pituitary hormones Mammogens I and II, or whether they may be ascribed to one or other of the well-characterized hormones known to be secreted by the anterior lobe. On this point, Mixner, Bergman & Turner (1942) believe that the lobule-alveolar growth-promoting mammogen is distinct from prolactin, thyrotrophin and gonadotrophin.

There is indeed some reason to believe that of the known anterior-lobe hormones, prolactin (anterior-pituitary lactogenic hormone) may be the one most likely to be concerned with mammary growth. Lyons & Catchpole (1933) claimed that prolactin would promote growth of the mammary tissue, and more convincing evidence has since been provided by Lyons (1942), who reported localized alveolar hyperplasia in response to intra-mammary-duct injections of pure prolactin in the rabbit. Moreover, fairly extensive mammary growth in hypophysectomized animals in response to combined treatment with oestrogen and prolactin has been reported (Gardner & White, 1941, 1942 ; Gomez, 1942 ; Lyons, 1943). Gardner & White have indeed put forward the view that prolactin sensitizes the mammary gland to the action of ovarian hormones, a theory which, implying as it does a synergism between anterior-pituitary hormones and ovarian steroids, without excluding a direct action of the latter on the mammary epithelium, has something to commend it.

3. Adrenal Cortex[2]

The possibility that the adrenal cortex might influence mammary development was first indicated when Van Heuverswyn, Folley & Gardner (1939) showed that one of the cortical hormones, deoxycorticosterone, would promote growth of the mammary ducts in mice. In general confirmation of the mammogenic effect of deoxycorticosterone, it was later found that this hormone would stimulate alveolar growth in the monkey (Speert, 1940b), guinea-pig (Nelson, Gaunt & Schweizer, 1943) and, in the presence of oestrogen, in the mouse (Mixner & Turner, 1942b, 1943). No observations of the effects of 11-oxygenated cortical steroids on mammary development have yet been made, but the results with the 11-deoxy hormone might well provide an explanation of clinical cases of gynaecomastia associated with tumours of the cortex, and of gynaecomastia following treatment of males with cortical extracts.

On the other hand, the few studies which have been made on the effects of adrenalectomy on mammary-gland structure have given discordant and not very dramatic results. Results which may be interpreted as indicating (but perhaps not decisively) that adrenalectomy is followed by increased mammary growth have been reported by Butcher (1939) and Reeder & Leonard (1944), but Cowie & Folley (1944, 1947) found that, when such mammary changes occurred, they were in the direction of regression.

Since one of the adrenal-cortex hormones is capable of causing mammary growth, the possibility that the mammogenic activity exhibited by crude anterior-pituitary extracts might be due, at any rate partly, to the presence therein of adrenotrophin must be considered, particularly since Nelson (1941b) has observed mammary growth in hypophysectomized-gonadectomized rats following injections of adrenotrophin. Cowie & Folley (1947), using a semi-quantitative method devised by them for statistical study of mammary development in the rat, found that while the mammogenic effect of crude anterior-pituitary extract was often upset by adrenalectomy, it was to a considerable extent independent of the adrenal cortex and hence not by any means wholly ascribable to adrenotrophin.

On the basis of present knowledge then, there is no reason to believe that the cortex exerts any important influence on normal mammary development.

4. Placenta

In pregnant mice from which the foetuses and ovaries (Newton & Lits, 1938) or foetuses and hypophysis

[2] Since this review was written papers by Chamorro have come to hand in which it is reported that adrenalectomy had no effect on mammary structure in adult rats (Chamorro, 1946) and that administration of deoxycorticosterone caused, at best, only slight growth-responses in the mammary gland of the castrated male mouse (Chamorro, 1945).

(Newton & Beck, 1939) are experimentally removed, when the placentae are retained until autopsy the mammary glands resemble those characteristic of the pregnant animal at a corresponding stage of gestation. If the placentae are aborted, however, the mammae regress. There is an obvious temptation to interpret these facts as showing that, in the absence of the hypophysis, the placenta is able to promote mammary growth. The fact that in species which do not abort following hypophysectomy during pregnancy the mammae appear fairly normal at term, sometimes even to the extent of secreting milk for a short time (see Selye, Collip & Thomson, 1933b; Newton & Beck, 1939; Newton & Richardson, 1941; Gardner & Allen, 1942, for the mouse: Selye, Collip & Thomson, 1933a; Pencharz & Long, 1933; Jeffers, 1935, rat: and Pencharz & Lyons, 1934; Desclin, 1939, guinea-pig), has suggested to some that in these circumstances the placenta may take over the function of the missing hypophysis as far as it is concerned with mammary growth and the initiation of milk-secretion.

Lyons (1944) has recently reported results which suggested to him that the placenta may secrete a hormone which synergizes with ovarian hormones in causing mammary growth. In rats hypophysectomized early in pregnancy, oestrone and progesterone caused continued mammary development only in the presence of the placenta. A somewhat similar conclusion was reached by Leonard (1945).

The majority of the above-mentioned workers seems, however, to have neglected the distinction, emphasized at the beginning of this review, between the mammary-growth phase largely confined to the first half of pregnancy and the secretory phase (accompanied by an apparent, but probably not real, increase in alveolar tissue) characteristic of the second half of pregnancy. It seems likely that, in the absence of the hypophysis, the placenta may assume an hypophyseal function in that it secretes a hormone or hormones capable of initiating the secretory phase and thus preventing mammary regression. But this is hardly the same thing as promoting mammary growth, and the whole question of placental influence on mammary development obviously needs further investigation with this point in mind.

5. Thyroid

Observations of earlier workers on reproduction in thyroidectomized rats and mice suggest that mammary growth can occur in the absence of the thyroid, but these studies were of such a nature that they could not, nor were they intended to, provide detailed information on the structure of the mammary gland. More-recent studies, directed specifically to this end, such as those of Leonard & Reece (1941), Smithcors & Leonard (1942), Mixner & Turner (1942c, 1943), and Chamorro (1946) (see also Petersen, Knodt, Ludwick & Pomeroy, 1944), suggest that thyroidectomy exerts a profound influence on mammary development, most probably by modifying the response of the mammary tissue to the stimulus of hormones which promote mammary growth. Thus, in the absence of the thyroid, oestradiol appears to promote alveolar growth rather than duct-growth in the rat (Smithcors & Leonard, 1942). In considering many of these results, the great difficulty, if not virtual impossibility, of achieving complete thyroid removal, at any rate in the rat (Folley, Scott Watson & Amoroso, 1942; Karnofsky, 1942), must not be overlooked.

Experiments on the effect on mammary growth of thyroid administration (Weichert & Boyd, 1934; Cohen, 1935; Gardner, 1942; Mixner & Turner, 1942c, 1943) also indicate that, in keeping with the role of the thyroid gland as a regulator of body metabolism, the level of thyroid activity exerts an indirect influence on mammary development in the manner postulated above. The indirect nature of this influence is underlined by Gardner's (1942) finding that thyroid-feeding accelerated mammary growth in intact, but not in gonadectomized, mice.

6. Conclusions

In this necessarily brief review it has been possible to consider only certain aspects of the general problem of mammary growth; even within these limits, citation and discussion of many important papers have had to be omitted. Nevertheless, the considerations that have been put forward permit certain broad conclusions. The ovarian hormones, oestrogen and progesterone, are undoubtedly the principal primary agents which evoke mammary growth. Whether or not they accomplish this through the agency of specific anterior-pituitary mammogens remains to be seen, but it does seem established that the anterior pituitary may secrete factors which can cause mammary development in the absence of both the ovaries and adrenals, and pituitary influence may well be essential for the complete expression of the mammary-growth-stimulating action of oestrogen and progesterone. The influence of the thyroid on mammary development is probably indirect; that of the placenta problematical.

In most, perhaps all, species, both oestrogen and progesterone, presumably in a well-adjusted ratio, are necessary for complete and normal mammary development, but in certain species oestrogen alone evokes development of a considerable amount of alveolar tissue, which however is not necessarily normal structurally. This can be accomplished most spectacularly in the ruminant, in which results of potential practical significance have been obtained.

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ENDOCRINE CONTROL OF THE MAMMARY GLAND

II. Lactation

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1 Anterior-pituitary lactogenic hormone (prolactin)
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Modern developments in the field of lactational endocrinology date from the discovery by Stricker & Grueter (1928) that lactation could be initiated in pseudopregnant rabbits, after ovariectomy, by injection of anterior-pituitary extracts. This important discovery, which carried the then novel implication that the intervention of a positive hormonal stimulus is necessary for the initiation of lactation, was quickly confirmed in its essentials in a variety of species, the only desideratum being the presence in the test-animal of a sufficiency of responsive mammary tissue. The crucial importance of the pituitary for mammary secretion was also soon demonstrated by numerous experiments in which it was shown that its absence was incompatible with the initiation or maintenance of lactation (see reviews by Nelson, 1936; Turner, 1939; and Folley, 1940).

1. Anterior-Pituitary Lactogenic Hormone (Prolactin)[1]

Evidence was soon forthcoming which suggested that the lactogenic properties of anterior-pituitary extracts were not associated with the three, perhaps four, anterior-pituitary hormones—growth hormone, thyrotrophic hormone and the one or two gonadotrophic hormones—which at the time were emerging as fairly well-characterized entities, and the idea arose that a new hormone (lactogenic hormone or prolactin) was responsible.

The chemical studies leading to the recognition of the existence of this new hormone were greatly aided by its early identification by Riddle, Bates & Dykshorn (1933) with a constituent of anterior-pituitary extracts which causes enlargement and secretion of the crop-glands of the dove and pigeon. This interesting discovery provided the basis for a convenient and apparently specific quantitative method of assay of prolactin. The assay method described by Riddle *et al.* (1933) and adopted with minor modifications by several subsequent workers, involved systemic injection and weighing of the crop-glands. A "micro" or "local" method, in which the test-solution is injected intradermally directly over the crop-gland, and which enables the detection and even quantitative measurement of much smaller amounts of hormone than can be assayed by the systemic method, was introduced by Lyons & Page (1935) for the assay of prolactin in urine, and the principle was used in various forms by subsequent workers for, among other purposes, determining the prolactin potency of pituitaries of small animals (for references to clinical studies of prolactin excretion, see Meites & Turner, 1941). Attempts have been made to develop mammalian methods of prolactin assay, which would obviously be preferable from the theoretical point of view, but, judging from the fact that pigeon-methods still hold the field, so far without conspicuous success. Review articles on the assay of prolactin have been published by Bates (1937), Lyons (1937) and Riddle & Bates (1939), and the interested reader might also consult Bergman, Meites & Turner (1940), Folley, Dyer & Coward (1940), Meites, Bergman & Turner (1941), Lyons (1941) and Hall (1944a, 1944b) for details regarding various methods of prolactin assay, quantitative comparisons between various types of unit and other practical information.

Two useful methods for partial purification and concentration of prolactin, respectively involving extraction of pituitary glands with acid acetone (Lyons & Catchpole, 1933) and alkaline alcohol (Bates & Riddle, 1935), were evolved at an early stage, but more recently it has been possible to prepare prolactin as a pure amorphous (Li, Simpson & Evans, 1942) and even crystalline (White, Catchpole & Long, 1937; White, Bonsnes & Long, 1942) protein, exhibiting an activity of 20-30 international units per mg. Prolactin was the first anterior-pituitary hormone to be isolated in the pure state, and recently considerable information concerning its chemistry has accrued from the studies of groups led by Evans at California and White at Yale. For further information on chemical aspects the reader should consult recent excellent reviews by White (1943, 1946) and, for a general account of prolactin, a comprehensive review by Voss (1941).

2. Prolactin as a Specific Lactogenic Hormone

The remarkable ability of anterior-pituitary extracts containing, as judged by the pigeon crop-gland test, prolactin, to initiate lactation in animals possessing suitable mammary tissue, a property which, it was soon manifest, could be enhanced by chemical purification, gave rise to the current belief, widely held, that prolactin is the sole and specific lactogenic hormone. In other words, most workers in this field (*e.g.* Bergman & Turner, 1940; Lyons, 1941) at present adhere to a theory which postulates a single anterior-pituitary hormone, prolactin, as being responsible

[1] For a few years after its discovery this hormone was variously called *prolactin* (Riddle), *galactin* (Turner) and *mammotropin* (Lyons). Later, the terms *lactogen* and *lactogenic hormone* were introduced, and the latter is now widely used in the USA. In this review, *prolactin*, the term which is customarily used in Britain, will be adopted.

for the initiation of lactation. At the same time it has been recognized that participation in lactogenesis may not be the only, nor necessarily the most important, biological function of prolactin (e.g. Riddle & Bates, 1939).

We must take note, however, of the modern tendency to define the specific biological properties of anterior-lobe hormones in terms of the responses evoked in hypophysectomized animals, the argument being that in intact animals the intervention of endogenous pituitary hormones may obscure the response-picture. If, in keeping with this conception, lactogenic hormones are defined as anterior-pituitary hormones which will initiate lactation in *hypophysectomized* animals possessing suitably-responsive mammary tissue, there is reason to doubt the adequacy of the single-lactogenic-hormone theory. For, while crude anterior-pituitary extracts will initiate lactation in the absence of the hypophysis (McPhail, 1935a, 1935b; Houssay, 1935a; Gomez & Turner, 1936a, 1937a; Nelson & Gaunt, 1936, 1937a), partially-purified prolactin is ineffective (Gomez & Turner, 1936a, 1937a; Nelson & Gaunt, 1936, 1937b). Evidently some other anterior-lobe hormone or hormones, missing from the partially-purified prolactin-preparations, must co-operate with prolactin in initiating lactation in hypophysectomized animals, and it happens that adrenotrophin may be specially important in this connexion, since lactation can be initiated in hypophysectomized guinea-pigs by administration of partially-purified prolactin (and sometimes glucose) together with adrenal-cortex extract (Gomez & Turner, 1936b, 1937a; Nelson & Gaunt, 1936, 1937a, 1937b), certain cortical steroids (Nelson, Gaunt & Schweizer, 1943) or adrenotrophin (Gomez & Turner, 1937a, 1937b; Nelson & Gaunt, 1937b).

Two points are worth noting about these results. First, they relate only to the guinea-pig, an animal in which it is particularly easy to stimulate lactogenesis (see Nelson, 1936), so that its lack of response to partially-purified prolactin is the more remarkable. Second, Fredrikson (1939) has reported positive lactational responses to purified prolactin in completely hypophysectomized rabbits, so that it seems desirable that the above-mentioned experiments should be repeated on other species, preferably with the highly-purified pituitary-hormone preparations now available. But if they are acceptable, then as Folley & Young (1941) in a discussion of the status of prolactin as a lactogenic hormone have pointed out, the results just discussed can mean only that prolactin and adrenotrophin must both be considered as lactogenic hormones, for either will presumably initiate lactation in the presence of the other. Thus, in place of the conventional single-lactogenic-hormone theory, Folley & Young (1938, 1940, 1941) put forward the conception of a lactogenic hormone-complex, a view in which Riddle (1940) apparently concurs. Two members of this hormone-complex appear to have been identified as we have seen, while others may or may not remain to be discovered. The fact that in lactogenesis prolactin may exert a direct action on the mammary gland, as indicated by the elegant experiments of Lyons (1942) who demonstrated a direct and localized effect of prolactin on the alveolar epithelium, while adrenotrophin almost certainly plays an indirect role in that perhaps it governs, through the cortical hormones, the supply of milk-precursors (see section on Adrenal Cortex, below), does nothing to invalidate the above argument.

As evidence for the existence of a single specific lactogenic hormone, prolactin, Bergman, Meites & Turner (1940) cite results of prolactin assays carried out on pigeons and mammals with an anterior-pituitary extract at different stages of purification. The ratio of the potencies given by the two types of assay was hardly affected by purification. This might merely mean, however, that the components of a lactogenic hormone-complex were concentrated in the same proportions. Further, Bergman & Turner (1940) have pointed out that an anterior-pituitary extract can be fractionated into two parts, one containing the prolactin and possessing high lactogenic activity in intact mammals, the other containing certain other anterior-lobe hormones and exhibiting very little lactogenic activity even in comparatively large doses. For discussion of these results in relation to the single- and multiple-lactogenic-hormone theories, the reader is referred to Folley & Young (1941); it suffices to point out now, that since the experiments of Bergman & Turner relate to rabbits possessing pituitary glands, they are hardly relevant to the point at issue. More recently Hurst & Turner (1942) appear to accept the view that more than one anterior-pituitary hormone may be concerned in lactogenesis, at least in the mouse.

3. Galactopoietic Action of the Anterior Pituitary

In the present state of knowledge it seems desirable to use separate terms in respect of the initiation of lactation and its stimulation once established. Following Folley & Young (1940) and Bergman & Turner (1940), the terms "*lactogenesis*" and "*galactopoiesis*" are used in this review to designate these two processes respectively.

Investigations on lactating ruminants have clearly shown that anterior-pituitary extracts exert a marked but temporary galactopoietic effect, the important point being that unfractionated extracts are much more active per unit of prolactin than preparations of purified prolactin, both when responses to single injections (Azimov & Krouze, 1937; Folley & Young, 1938) or repeated injections (Folley & Young, 1940) are measured. Studies of the galactopoietic activities of anterior-pituitary extracts in relation to certain of their other biological properties (Folley & Young, 1938, 1939, 1940) indicated some parallelism between the galactopoietic and glycotropic (anti-insulin) activities of the series of extracts used, so that a complex of anterior-pituitary factors (one member of which is, of course, prolactin) rather than a single hormone would appear to be involved in the maintenance of lactation as well as in its initiation.

Galactopoiesis is discussed in another paper[2] of this series (Young, 1947), to which the reader is referred, and it remains only to consider briefly the bearing of this question on the clinical use of prolactin. Prolactin has been used for the treatment of hypogalactia (for reviews see Riddle, 1940; Robinson,[3] 1947; and Voss, 1941) with conflicting and often disappointing results. Quite apart from the fact that hypogalactia may not necessarily be due to anterior-pituitary hypofunction, such a lack of agreement might be expected from the considerations briefly outlined above, since the extracts used have been standardized in terms of prolactin content as measured by the pigeon-method and used on the tacit assumption that this is a measure of

[2] [*BMB* 1104]
[3] [*BMB* 1106]

galactopoietic power. As the investigations of Folley & Young show, this is certainly not the case.

4. Suckling-Stimulus and Prolactin Secretion

Though no one today believes in the existence of secretory nerve-fibres passing to the mammary gland, it has been suggested that nervous influences may be concerned in the secretion of milk by remote control, as it were, in so far as the release of prolactin from the pituitary may to some extent depend on nervous stimuli.

Selye, Collip & Thomson (1934) give a full discussion of this question, which was opened by such observations as those of Selye (1934), who found that in lactating rats in which some nipples at least were suckled, the histological picture of cessation of secretory activity and involution, characteristic of weaning, was absent from glands from which egress of milk was prevented by duct-ligation, or of which suckling was rendered impossible by excision of the nipple. Their interpretation ascribes these effects to reflex secretion of prolactin, acting systemically on all glands alike, in response to the suckling-stimulus. These results have in broad outline been confirmed by Williams (1941).

Other results in general accord with such an interpretation have been reported. Thus, mammary involution in non-suckled glands can be retarded by utilizing the irritant action of turpentine, applied to the nipples, as a substitute for the suckling-stimulus (Hooker & Williams, 1940), or by injections of prolactin (Hooker & Williams, 1941). If one accepts the view that the pituitary-prolactin potency is a measure of prolactin secretion, the results of Meites & Turner (1942a, 1942d) could also be cited. They found more prolactin in the hypophyses of suckled rats and rabbits than in those of non-suckled ones. Finally, we have the observations of Selye & McKeown (1934a, 1934b), who showed that pseudopregnancy (accompanied by mammary development) could be induced in cyclic rats and mice by application of the suckling-stimulus, but only in the presence of the ovary. These last observations fit into the general picture, provided that we accept the luteotrophic role for prolactin (e.g. Evans, Simpson & Lyons, 1941; Astwood, 1941), evidence for which is growing.

5. Oestrogen

Dating from the experiments of Parkes & Bellerby (1927), who showed that administration of oestrogen to lactating mice depressed the growth-rate of the sucklings, numerous experiments on small animals, in which lactational performance can be measured only by a similar indirect technique, have been held to testify that oestrogen exerts an inhibitory action on lactation. These experiments are referred to in reviews by Nelson (1936), Turner (1939), Folley (1940) and Petersen (1944), and are discussed in papers by Folley & Kon (1937), Edelmann & Gaunt (1941) and Meites & Turner (1942a).

Doubts as to the reality of the apparent inhibiting action of oestrogen on lactation have been expressed, notably by Abarbanel & Goodfriend (1940), who hold that the beneficial results following the administration of oestrogen to lactating women, who for one reason or another must not be allowed to lactate, are due rather to relief of painful engorgement (a condition ascribed to lymphatic and venous stasis) than to inhibition of milk-secretion, which, it is believed, does not occur in spite of the oestrogen if suckling is continued (see also Fauvet, 1943). Meites & Turner (1942a) also question whether oestrogen inhibits lactation, principally because the administration of oestrogen, even in large doses, causes an increase, not a decrease, in the prolactin content of the pituitary.

However, despite the criticisms that may be levelled against the results with small animals in which lactational performance can be inferred only by an indirect and not unobjectionable technique, experiments on ruminants, in which milk-yield can be directly and accurately measured (Folley, 1936; Waterman, Freud & Vos-de Jongh, 1936; Folley, Scott Watson & Bottomley, 1941a; Stanley & Owen, 1941; Mixner, Meites & Turner, 1944; Folley, Malpress & Young, 1945), appear to provide good evidence that sufficient doses of oestrogen tend to suppress lactation even though milking is continued. The fact that the doses of oestrogen necessary may have been "unphysiological" does not affect the principle at issue.

Besides the possible inhibitory action on lactation just considered, oestrogen, as is now known, is capable of exerting quite opposite effects. In fact, there now exists an impressive body of evidence indicating that under appropriate conditions oestrogen may function both as a lactogenic and a galactopoietic agent.

Even while the opinion that the role of oestrogen in lactation was purely inhibitory was still widely and authoritatively held, certain workers (e.g. Frazier & Mu, 1935) had observed evidence of secretion in the experimentally-developed mammae of small animals subjected to prolonged oestrogen treatment. The most striking and unequivocal evidence of the lactogenic effect of oestrogen has however been obtained in more recent studies on ruminants.

The results of Folley, Scott Watson & Bottomley (1940, 1941b), who surprisingly found that oestrogen would not only evoke udder-growth in the goat, but also the initiation of copious lactation, indicated unequivocally for the first time, as far as the present writer is aware, the necessity for a revision of classical concepts (ably expounded by Nelson, 1936) which assigned to oestrogen the dual role of stimulating mammary development while holding secretion in check. These results were quickly confirmed and extended in the goat (Lewis & Turner, 1940, 1941, 1942; Mixner & Turner, 1943; Folley, Malpress & Young, 1945), sheep (Peeters & Massart, 1947) and ox (Walker & Stanley, 1940, 1941; Reece, 1943; Folley & Malpress, 1944a, 1944b; Folley, Stewart & Young, 1944; Hammond & Day, 1944; Parkes & Glover, 1944; Day & Hammond, 1945; Spriggs, 1945). The whole question is discussed more fully in an accompanying article[4] (Malpress, 1947).

These interesting and even spectacular findings testify to the ability of oestrogen to evoke certainly lactogenesis, and probably also galactopoiesis, since a constant feature was the compatibility of a fast-increasing milk-yield with the continued administration of oestrogen. In point of fact, evidence of a galactopoietic effect of oestrogen had already been obtained by Folley (1936) in experiments of quite a different nature, galactopoiesis manifesting itself

[4] [*BMB* 1105]

by a prolonged increase in the concentration of milk-solids (the " enrichment " effect). Later investigation of the " enrichment " effect has shown that an increased secretion of major milk-constituents is involved, and that there is no question of the milk-composition reverting towards that of colostrum (Folley & Scott Watson, 1938 ; Folley, Scott Watson & Bottomley, 1941a ; Spielman, Ludwick & Petersen, 1941).

As to the mechanism of these lactogenic and galactopoietic effects, it seems most probable that they are mediated by the anterior pituitary, which must be supposed to release the lactogenic and galactopoietic hormone-complexes (which incidentally, may or may not be identical, but see Folley & Young, 1941) in response to the stimulus of oestrogen or perhaps of metabolic derivatives thereof. Folley (1941) in a discussion of the role of oestrogen in lactation, has suggested that the oestrogen-threshold for pituitary stimulation is probably lower than that for inhibition, so that the factor determining whether stimulation or inhibition shall prevail would be the level of oestrogen in the body-fluids.

6. Adrenal Cortex

Experiments on the initiation of lactation in the absence of the hypophysis, discussed above, have emphasized the importance of the pituitary-adrenal mechanism in this connexion and led to the conclusion that the functional integrity of the cortex is essential for lactogenesis. Information on which of the cortical functions is critical for lactogenesis comes from the work of Nelson *et al.* (1943), whose results indicate that the cortical steroids which together with prolactin initiate lactation in hypophysectomized animals are those which promote gluconeogenesis (11-oxygenated steroids) rather than those related to electrolyte metabolism (11-deoxy steroids).

The role of the adrenal cortex in lactation has also been studied in adrenalectomized animals. Early investigations indicated that normal lactation was impossible in the absence of the adrenals (for references see Nelson & Gaunt, 1937a.). From more recent work on the rat it is clear that though adrenalectomy seriously interferes with lactation, it does not abolish it completely[5] (Gaunt 1941 ; Gaunt, Eversole & Kendall, 1942 ; Folley & Cowie, 1944 ; Cowie & Folley, 1947a). It also appears that some alleviation of the lactational failure may be afforded by sodium chloride (Gaunt & Tobin, 1936 ; Levenstein, 1937 ; Folley & Cowie, 1944 ; but see Tobin, 1939) and more by administration of cortical extracts (Gaunt & Tobin, 1936 ; Gaunt *et al.* 1942 ; but see Folley & Cowie, 1944).

Investigations of the ability of various crystalline cortical steroids to maintain lactation in adrenalectomized rats have, however, given rise to a rather puzzling situation. Gaunt *et al.* (1942) achieved only partial and irregular lactational responses with 11-deoxycorticosterone, but complete restoration with 17-hydroxy-11-dehydrocorticosterone, and were thus led to conclude that while the restoration of a normal electrolyte metabolism may be helpful for the maintenance of lactation, the limiting factor for maximal secretion is a sufficiency of those cortical factors (the 11-oxygenated steroids) which are concerned with carbohydrate and protein metabolism. Folley & Cowie (1944), however, found that the 11-oxygenated steroids were inferior to 11-deoxycorticosterone for lactation-maintenance in their rats, and further studies have shown that the relative activities in this respect of the two types of steroid were unaffected by increasing the intake of protein (Cowie & Folley, 1947b) or sodium (Cowie, Folley, French & Greenbaum, 1947). Save in one exceptional experiment, however, (Cowie & Folley, 1947a), it has not been possible to achieve complete restoration of lactation in adrenalectomized rats with 11-deoxycorticosterone.

In a study of the arginase (an enzyme concerned in the formation of urea, and therefore a participant in gluconeogenesis) of the mammary gland, Folley & Greenbaum (1947a) were led to suggest that gluconeogenesis is an important element in the metabolism of the fully-lactating gland. Now, adrenalectomy appears to result in a decrease in the arginase not only of the liver (Fraenkel-Conrat, Simpson & Evans, 1943 ; Folley & Greenbaum, 1946) but also of the mammary gland (Folley & Greenbaum, 1946 ; Cowie *et al.* 1947), and it seems possible therefore that the impairment of lactation following adrenalectomy may be due, at least partly, to the loss of milk precursors which arise from the deamination of amino-acids in the mammary tissue[6].

Finally, brief consideration must be given to the possibility of the existence of a specific lactation-hormone of the adrenal cortex. The presence of such a hormone, called cortilactin, in adrenal-cortex extracts was postulated by Brownell, Lockwood & Hartman (1933) (see also Hartman, Lockwood & Brownell, 1933). Spoor, Hartman & Brownell (1941) claim that cortilactin is a pigeon-crop-stimulating hormone which plays no role in gluconeogenesis, but Hurst, Meites & Turner (1942) could detect no crop-stimulating activity in adrenal-cortex extracts. In view of the above-mentioned claims to have effected complete restoration of lactation in adrenalectomized rats with crystalline steroids, the existence of cortilactin must, until further evidence is forthcoming, be treated with reserve.

7. Thyroid

Experiments on the effect of thyroidectomy on lactation in various species have given no very clear picture. Interpretation of the results is complicated in the case of farm-animals by the effects of operative disturbances, which have been recognized by such workers as Grimmer (1918) and Graham (1934a), and in the case of the rat by the difficulty of effecting complete thyroid removal, and by the fact that the operation must involve the removal of the parathyroids (see Folley, Scott Watson & Amoroso, 1942 ; Cowie & Folley, 1945). There is no space to consider these studies here, but they have been briefly reviewed by Turner (1939), Folley (1940) and Petersen (1944). A critical appraisal leads to the general conclusion that in the absence of the thyroid, lactation can be initiated (on this specific point, also see Houssay, 1935b), and will proceed, but only at a reduced level and perhaps for a shorter time than normally.

[5] Recent paired-feeding experiments in the present author's laboratory indicate that part, but not all, of the lactational decline following adrenalectomy may be ascribed to the reduction of food-intake resulting from the operation (Cowie & Folley ; to be published).

[6] The decreases in liver and mammary-gland arginase-levels following adrenalectomy do not appear to be due to post-operative anorexia, since these changes have been confirmed in a paired-feeding experiment (Folley & Greenbaum, 1947b).

Studies of the effects on milk-yield of administration of thyroid hormone lead to the conclusion, which is in harmony with the role of the thyroid as a regulator of body-metabolism, that the intensity of lactation is to some extent dependent on the general level of activity of the thyroid gland. A temporary galactopoietic response following the administration of dried thyroid to one cow was reported as long ago as 1896 by Hertoghe (1896), but modern work on the galactopoietic effect of the thyroid hormone was initiated by Graham (1934a, 1934b), who observed marked increases in the yield of milk, and even greater increases in the yield of milk-fat, during the administration of dried thyroid gland, or thyroxine, to cows in declining lactation. The first adequate confirmation and extension of these results came from Folley & White (1936), who showed that thyroxine treatment does not hold up the normal decline of lactation, but merely raises the lactation-curve, temporarily, to a higher level, and that in addition to the increase in fat-content the non-fatty solids of the milk are also increased. They also found that thyroxine administration causes an immediate and dramatic decline in the concentration of alkaline phosphatase in the milk.

Further investigations of these galactopoietic responses have further defined their principal features (Herman, Graham & Turner, 1938; Hurst, Reece & Bartlett, 1940; Ralston, Cowsert, Ragsdale, Herman & Turner, 1940; Smith & Dastur, 1938) and essentially-similar results have been obtained by oral administration of iodocasein, a protein derivative which exhibits thyroidal activity, to lactating cows (Reineke & Turner, 1942a, 1942b; Blaxter, 1943, 1945a, 1945b, 1946; Reece, 1944; Van Landingham, Henderson & Weakley, 1944). These galactopoietic effects, advantage of which may well soon be taken in farm-practice, are dealt with further in an accompanying article[7] (Young, 1947).

8. Posterior Pituitary

Extracts of posterior pituitary exert a rapid but fleeting action on the mammary gland. Within a few seconds of the intravenous injection, shortly before her normal milking-time, of posterior-pituitary extract into a lactating cow or goat, there is a sudden, marked increase in the pressure of milk in the udder-cisterns, with which is associated the possibility of obtaining somewhat more milk than would be expected on the basis of previous milkings. If the injection is given to a lactating animal with a cannulated teat, its effect is quickly manifested by a temporary increase in the flow of milk from the cannula.

This response to posterior-pituitary extract was discovered by Ott & Scott (1911) and subsequent study of it (see references cited by Turner & Slaughter, 1930; Ely & Petersen, 1941; and Petersen, 1944) has corrected the early impression that true galactopoiesis was involved. In order to understand the nature of the effect of posterior-lobe extract on the mammary gland it is necessary to appreciate the distinction between two quite separate phenomena, the secretion of milk (which itself may be regarded as comprising two sub-phenomena, the synthesis of milk and its passage from the cytoplasm of the epithelial cells into the alveolar lumen) and the discharge or withdrawal of pre-formed milk from the mammary gland (see accompanying article[8] by Folley, 1947). Consideration of all the available evidence leaves little room for doubt that posterior-pituitary extracts have no effect upon the secretion of milk (not at any rate primarily) but influence only the mechanism governing the discharge of milk from the mammary gland. Modern work (Ely & Petersen, 1941; Miller & Petersen, 1941; Shaw, 1942; Knodt & Petersen, 1944) has amply confirmed the observation of earlier workers that after an injection of posterior-pituitary extract into an animal which has just been completely milked-out, a further quantity of milk, unusually rich in fat, can be obtained, but a survey of the earlier results provides some indication of a tendency for the extra milk so obtained to be compensated for by a reduced yield at the next milking unless posterior-pituitary extract is again injected. In accordance with this, Gavin (1913) and Shaw (1942) found no indication that the average daily milk-yield of the lactating cow is increased during a period of repeated injections. On the other hand, Knodt & Petersen (1944) reported that in cows in declining lactation the rate of decline was somewhat diminished during a period in which, after each milking, the residual milk was made available by oxytocin injections. These authors, however, correctly ascribed their results not to a galactopoietic action of the oxytocin but to the beneficial effects on the function of the secretory cells of more efficient removal of milk from the alveoli.

Quite soon after the discovery of the effect of posterior-pituitary extract on the mammary gland, some workers (e.g. Heaney, 1913; Schäfer, 1915; Gaines, 1915) came to the conclusion, which in its essentials is accepted today, that the posterior-lobe extract favours the discharge of milk from the mammary gland by causing contraction of smooth-muscle cells, or other cells with similar contractile properties, present in the mammary tissue. The milk present in the lumina of the alveoli and the finest ducts (i.e. the major proportion of the milk present in the mammary gland), which is there tenaciously held presumably by capillary forces, is believed to be thereby squeezed under pressure down into the larger ducts and, in species in which these are present, the milk-cisterns, from which it readily flows during milking.

The nature of the cells in the mammary tissues which are supposed to contract under the influence of posterior-lobe extract is, however, at present not very clear. Swanson & Turner (1941) claim to have demonstrated, more conclusively than has previously been possible, the presence in the udder of the lactating cow of cells in close association with the alveoli which have the appearance and staining-properties of smooth-muscle fibres. This claim, if confirmed, would do much to resolve any difficulties regarding a possible mechanism for the effect under discussion. If, however, these authors are referring to myo-epithelial cells (the so-called basket-cells), it should be pointed out that the contractile properties of these cells have never yet been demonstrated, having only been inferred by analogy with the properties of smooth-muscle cells (see for instance Babkin, 1944). Nevertheless, the available evidence is such that there can be little doubt that injection of posterior-pituitary extract causes some contraction of the mammary tissues, and this was demonstrated in man in a particularly simple, yet effective way by Heaney (1913), who appears

[7] [*BMB* 1104]

[8] [*BMB* 1102]

to have been the first clearly to enunciate the currently-accepted view of the action of posterior-pituitary extracts on the mammary gland.

The oxytocic principle of the posterior lobe seems to be more active in its effect on the mammary gland than the pressor principle (Ely & Petersen, 1941) though Turner & Cooper (1941), who attempted to devise a quantitative assay-method based on this response, found more activity in posterior-pituitary extracts rich in the pressor principle than they expected on the basis of the amount of oxytocin present, and in consequence they put forward the suggestion that the effect might be due to the combined action of the oxytocic and pressor principles, or even perhaps to some third factor present in both types of posterior-pituitary extract.

The question whether the posterior pituitary plays any physiological role in the normal process of suckling or in artificial milking immediately presents itself. This possibility which has recently been put forward, and in favour of which a certain amount of rather circumstantial evidence has been adduced, is discussed in an accompanying article (Folley, 1947), to which the reader is referred. It remains only to add in this connexion that the observations of Smith (1932) and Houssay (1935a) indicate that lactation is possible in the absence of the posterior hypophysis, while Gomez (1939, 1940) found that hypophysectomized rats receiving replacement-therapy lactated better if regular injections of posterior-pituitary extract were given.

9. Initiation of Lactation

Though, as is well known, secretion begins in the mammary gland mid-way through pregnancy, copious lactation usually does not begin until shortly after parturition, save in what must be regarded as exceptional cases, such as in goats belonging to " deep-milking " strains which often secrete appreciable quantities of milk even before mating. The mechanism governing the initiation of copious lactation in the ordinarily-understood sense has been the subject of much speculation. Practically all theories which have been put forward postulate an inhibitory influence operating during pregnancy, variously identified with the placenta, the corpus luteum of pregnancy, the distension of the uterus and so forth, the removal of which at parturition permits the full expression of the secretory activities of the mammae.

We need consider only modern theories. The first of these to take account of the lactogenic function of the anterior pituitary was put forward by Nelson, who has ably summarized (Nelson, 1936) much evidence in support of it reported in his earlier papers. Briefly, the theory holds that oestrogen, probably of placental origin, holds secretion in check during pregnancy by inhibiting the secretion of prolactin, an action probably reinforced by an inhibitory influence exerted directly on the mammary gland. The fall in the level of circulating oestrogen at parturition permits the release of prolactin by the hypophysis and hence the initiation of full lactation.

This theory has been criticized by Meites & Turner (1942a), who are not convinced that oestrogen, at any rate in physiological titres, does in fact inhibit lactation. They adduce results which indicate that oestrogen even in enormous doses always causes an increase, never a decrease, in the prolactin content of the pituitary. This provides them with the starting-point for a new theory (Meites & Turner, 1942a, 1942b, 1942c, 1942d) according to which an increase in the hypophyseal secretion of prolactin (deduced from observed increases in pituitary prolactin-potency in small animals) is the decisive factor for the initiation of lactation. During pregnancy, the oestrogen known to be circulating in large amounts is prevented from exerting its effect on the hypophysis by the overriding antagonistic action of progesterone, an influence which is eliminated at parturition. This theory is thus a modern derivative of older theories which regarded the initiation of lactation as a progesterone-withdrawal phenomenon, but is more detailed in its exposition of the supposed mechanism involved.

The evidence in favour of this ingenious theory cannot be considered in detail here; it must suffice to say that much of it is based on increases, or lack of them, in the pituitary prolactin-content, in small animals, observed under various experimental and physiological conditions, and in particular an increased pituitary prolactin in response to oestrogen and following parturition, which stands in contrast to the absence of effect when sufficient progesterone is given together with oestrogen.

Certain objections may be raised against this theory however. Limitation of space precludes adequate discussion, but the more cogent can be briefly indicated. The theory concentrates on prolactin as the sole anterior-lobe lactogenic hormone while, as we have seen, the status of prolactin in this respect is somewhat equivocal. Indeed, Hurst & Turner (1942) have admitted that in the mouse, at any rate, other hormones must also be involved in the initiation of lactation. More serious is the fact that the adequacy of the method used by Turner and his colleagues for measuring changes in the prolactin potency of the pituitary in small animals, on the reality of which the validity of the theory depends, is open to question (Hall, 1944b). Moreover, even if the observed changes are real, they may merely reflect storage-phenomena due to inhibition of release rather than increased secretion of prolactin. Finally, it is doubtful whether the high gravimetric progesterone/oestrone ratios found necessary by Meites & Turner (1942b) for the suppression of the oestrogen effect actually obtain during pregnancy. Very much lower ratios were found to be necessary for optimal mammary growth, which is a typical pregnancy phenomenon (Scharf & Lyons, 1941).

Nevertheless, if the Meites-Turner theory must, for the reasons stated above, be treated with reserve for the present, it must be remembered that the phenomenon of oestrogen-induced lactation, discussed in a previous section of this article, inevitably leads to the conclusion that relatively-low levels of circulating oestrogen are, as suggested by Folley (1941), capable of evoking the secretion by the hypophysis of the lactogenic and galactopoietic hormone-complexes. It may be that during pregnancy the oestrogen levels are indeed high enough partially to inhibit hormone secretion by the anterior lobe, and that at parturition the oestrogen level falls through the region between the thresholds for pituitary inhibition and stimulation, thus causing release of sufficient of the relevant hormone-complexes to bring the mammae into full function (see Folley & Malpress, 1947).

Finally we may mention the views of Petersen (1944), which take into account the fact that the secretory phase is established at mid-pregnancy or thereabouts. Petersen ascribes the copious postpartum flow of milk to the action

of oxytocin, circulating at that time, which causes expulsion of the contents of the alveoli and finest ducts, after which full secretion is maintained by the stimuli of suckling or milking (see accompanying article by Folley, 1947).

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THE NERVOUS SYSTEM AND LACTATION

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1 Sympathectomy and lactation
2 Suckling-stimulus and milk-secretion
3 Discharge or withdrawal of milk from the mammary gland : physiology of milking
References

Contemporary interpretation of much of the earlier work on the physiology of lactation was often subject to a certain amount of confusion because of failure to recognize the distinction between the formation of milk and the discharge or withdrawal of pre-formed milk from the mammary gland. Discussion of the relation of the nervous system to lactation will be greatly clarified if clear definitions covering this and other distinctions are laid down at the outset. The author therefore proposes that the total phenomenon which in this review is to be called *lactation* shall be considered as consisting of three sub-phenomena according to the following scheme.

(*a*) Synthesis of milk by the cells of the alveolar epithelium

(*b*) Passage of milk from the cytoplasm of the mammary epithelial cells into the alveolar lumen — (A) Milk-secretion

(B) Discharge or withdrawal of milk from the mammary gland

} Lactation

Where such terms as *lactation*, *milk-secretion*, *and milk-discharge* are used in this article, they are used advisedly and in accordance with this scheme.

In the era before the rise of modern endocrinology, the attention of lactational physiologists was naturally concentrated on the possible role of the nervous system in lactation. The early experiments in which attempts were made to denervate the mammary gland, tended to indicate that the growth and function of the mammary gland were independent of the nervous system and must be considered as

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being under the control of humoral influences. For reviews of these early experiments the reader is referred to Basch (1906) and Turner (1932). Perhaps the most conclusive experiments demonstrating the seeming paramount importance of hormonal factors in lactation were transplantation-experiments, a modern example of which is that of Stricker (1929).

With the rise of endocrinology as an independent and powerful science during the last two decades, and in view of the profound advances in lactational physiology which have resulted, there has perhaps been a tendency to overlook the part, important even if indirect, which neural mechanisms play in lactation. It is one of the aims of this review to show how modern work, revealing as it does an interplay between neural and hormonal mechanisms, is leading to a more balanced view which gives the important role played by the nervous system in lactation the recognition it deserves.

Though no one has yet provided any evidence whatever of the existence of secretory innervation of the mammary gland, there are several possible ways in which the nervous system may participate in the control of lactation. What seem to be the most important of the possibilities of more direct intervention are summarized below.

(*a*) The nervous system may affect lactation through its control of the calibre of the mammary blood-vessels on which would depend the rate of blood-flow through the mammary gland, and hence the rate of supply of milk-precursors to the secreting cells.

(*b*) The rate of secretion of hormones concerned in the initiation and maintenance of milk-secretion may be to some extent under nervous control. This may well apply particularly to certain anterior-pituitary hormones as will be seen later.

(*c*) Nervous influences may be concerned in the mechanism governing the discharge or withdrawal of milk from the mammary gland (i.e. in the natural process of suckling or artificial milking by hand or by machine). In this way also the nervous system may affect the total phenomenon of lactation, since a partial failure of the discharge-mechanism, leading to habitual incomplete withdrawal of milk from the gland, may well adversely affect milk-secretion and thus, by leading to its premature termination, amount to a failure of lactation. It is virtually certain, as will be seen later, that neural and even psychological factors are heavily involved at this point of the scheme outlined above, particularly in the domestic mammals kept by man as milk-producers, and are probably of outstanding importance in man himself.

Of these possibilities most is known about the last two, which will be considered in turn. Other possibilities such as the possible influence of nervous mechanisms on the permeability of the mammary alveolar cells to milk-precursors on the one hand, and milk-constituents on the other, lie at present entirely in the realm of speculation, since the existence of secretory nerve-fibres, comparable for instance with those regulating the activity of the cells of the salivary glands, has not been demonstrated. Before proceeding, however, to the two main themes of the present discussion, it is proposed to deal briefly with more or less recent experiments on the effect of sympathectomy on lactation, since these may be considered to be the modern analogues of the earlier experiments on the spinal denervation of the mammary gland.

1. Sympathectomy and Lactation

Fairly recently, a few experiments on the effect of sympathectomy on lactation have been carried out. Observations on lactation following sympathectomy operations have been reported by Cannon & Bright (1931) on one cat and one bitch, by Bacq (1932) on the rat, and by Simeone & Ross (1938) on the cat, as a result of which some commentators have shown a tendency to believe that sympathectomy causes impairment of lactation, although perhaps after some delay. There is no space here to give an analysis of these results, but it may be said that critical examination of the papers in question should convince the reader that in no case were sufficient animals involved, nor were the observations sufficiently numerous and definite, to exclude the possibility that any lactational disturbances or deficiencies observed subsequent to operative interference with the sympathetic ganglia were purely coincidental. It may therefore be concluded that at present there are no adequate grounds for any belief that sympathectomy interferes with lactation. The results of Houssay (1935a, 1935b) are in accord with this conclusion, since he reported that anterior-pituitary extract would initiate lactation in bitches from which the lumbar-sympathetic chains had been removed.

2. Suckling-Stimulus and Milk-Secretion

At the present time there is an ever-increasing interest in the factors which control the secretory activities of the pituitary gland, and already there is a certain amount of evidence which suggests that the secretion of some at least of the anterior-lobe hormones may be under the regulation of nervous stimuli. Of particular interest for our present purpose is the idea that the secretion of prolactin may be mediated by a nervous reflex in response to mechanical stimulation of the nipple.

It is well known that the weaning of the young is followed by rapid involution of the mammary gland, which was once believed to be due to the effects—perhaps chemical, perhaps mechanical—of the accumulation of milk. The observations of Selye (1934), however, first provided an indication that the removal of the suckling-stimulus is probably an even more important factor than non-removal of secretion in causing the onset of mammary involution. Conversely, it follows of course, that if Selye is right, the suckling-stimulus is continuously necessary for the maintenance of the functional integrity of the mammary gland. Selye (1934) found that in the rat, the prevention of the egress of milk by ligation of the main galactophores is not followed by the characteristic, rapid mammary involution if active suckling is continued. Further, involution was considerably retarded in glands which could not be suckled because of excision of the nipples, provided that other glands in the same animal, left with intact nipples, were suckled. H. Selye and his collaborators (Selye, Collip & Thomson, 1934, give a full discussion) were thus led to suggest that the suckling-stimulus initiates a nervous reflex which elicits the secretion of prolactin by the anterior lobe. In the case of the experimental animals just cited, the hormone is of course circulated to all glands alike, and thus maintains the secretory activities not only of normal glands but of glands from which the escape of milk has been surgically prevented.

The effect of the nursing-stimulus as distinct from the removal of secretion in retarding mammary involution has been confirmed in broad principle in mice by Williams (1941), who, however, observed less diminution of secretory activity in suckled glands from part of which no milk could be drawn because of appropriate duct-ligation, than in unsuckled (thelectomized) glands in the same animal. Earlier results of Hooker & Williams (1940) can also be considered as generally in accord with those of Selye, since although suckling of some mammae did not entirely prevent involution of other glands in the same mouse from which milk could not be withdrawn because of excision of the nipples, nevertheless involution of the thelectomized glands was much retarded as compared with post-weaning involution. Similarly in the rat, Grégoire (1947a) observed partial involution in suckled glands in which the galactophores were cut and in thelectomized glands in animals in which other (intact) nipples were suckled, but in neither case was the involution as rapid as after removal of the young. Weichert (1942), however, found that in rats with small litters which left some glands unsuckled, the latter underwent involution which was striking in comparison with the suckled glands; but it was still not as rapid as after weaning. In sum it may be said that while these more-recent studies indicate that the suckling-stimulus may not entirely prevent involution, even over relatively short periods, in unsuckled or unemptied glands, they confirm Selye's views to the extent that in general they show that the suckling-stimulus *per se* does retard mammary involution to a considerable degree.

Ingelbrecht (1935) has made some interesting observations (widely quoted no doubt because the elegance of the technique used appeals to the imagination of many commentators) which at first sight might appear to provide additional evidence that the mammary glands are responsive to a neurohormonal reflex of just the type we are discussing. He showed that if in the lactating rat the spinal cord is cut at such a level as to denervate the six posterior mammae, and the young are prevented from suckling the six anterior nipples, then they die from lack of milk. If, however, suckling of two of the thoracic glands with intact sensation is allowed, milk is copiously secreted by all glands alike, and the young thrive. In view of considerations later to be advanced, however, these experiments cannot be considered a critical test of the particular neurohormonal theory of Selye, since it is not certain how far they were concerned with the milk-discharge mechanism (a breakdown in which would perhaps lead to total lactational failure), rather than with failure of milk-secretion as such.

Hooker & Williams (1940) attempted to simulate the suckling-stimulus by the chemical irritation provided by the periodic application of turpentine to the nipples of weaned mice, and showed that not only was involution retarded in the glands corresponding to the treated nipples, but that similar effects were manifested to varying degrees in other glands of the same animal. Mixner & Turner (1941) confirmed the effect of turpentine, regularly applied to the nipple, in retarding mammary involution after weaning in mice, but considered the effects as local, due to hyperaemia, rather than as systemic.

A certain amount of additional experimental evidence may be cited which is in harmony with the concept that the suckling-stimulus causes reflex secretion of prolactin by the anterior pituitary.

In the first place, administration of prolactin to mice from which the litters have been removed retards mammary involution and tends to maintain the epithelium in a secretory state (Hooker & Williams, 1941; Williams, 1945). Somewhat similar results in rats have been reported by Grégoire (1947b), though Weichert (1942) found that prolactin failed to maintain complete activity in unsuckled glands in the rat even though other glands in the same animal were suckled.

Moreover, Reece & Turner (1937a, 1937b) found that, in the rat, application of the suckling-stimulus after a short period of non-suckling caused a decrease in the pituitary prolactin-potency as compared with unsuckled controls. This happened also in rats in which the galactophores had been ligated to prevent the escape of milk, thus showing that the effect was due to the milking-stimulus and not to milk-withdrawal. Similar results for the guinea-pig and rabbit were reported by Holst & Turner (1939). C. W. Turner and his school interpreted these results as indicating that suckling causes a discharge of prolactin from the pituitary. On the other hand, the long-term effect of regular suckling as contrasted with non-suckling appears to be an increase in the prolactin content of the hypophysis (Meites & Turner, 1942a, 1942b), which the Missouri group consider to be indicative of increased prolactin secretion. Thus, if one accepts their interpretation, regular suckling would appear to be necessary to maintain the high prolactin-output by the anterior lobe essential for milk-secretion. It should be pointed out, however, that if these results are to be accepted as evidence for the point at issue, one must be prepared to overlook Hall's (1944) criticisms of the methods used for the assay of the prolactin content of the small-animal pituitary and also the possibility that an increase in pituitary prolactin, even if real (but see Hall, 1944), may reflect merely a storage-effect, due to a decreased rate of release, rather than an increase in the rate of production. A further indication that suckling may increase the secretion of prolactin by the pituitary is however provided by the observations of Desclin (1945), who observed degranulation of the acidophils in the rat pituitary following suckling. It has been quite generally agreed that prolactin is secreted by the pituitary acidophils (Azimov & Altman, 1938; Schooley & Riddle, 1938; Friedman & Hall, 1941; Everett & Baker, 1945), though recently it has been claimed that a special type of acidophil, the carminophil cell, is involved (Dawson, 1946).

One further observation which may be fitted into the general picture may be mentioned. Selye & McKeown (1934a, 1934b, 1934c) found that application of the suckling-stimulus to normal, cyclic female rats and mice induced a condition reminiscent of the condition of pseudopregnancy evoked by sterile copulation or cervical stimulation, in that the oestrous cycles were interrupted by prolonged dioestrous periods during which mammary growth occurred. These phenomena occurred only in the presence of the ovary. This condition of "suckling pseudopregnancy" which, it is interesting to note, Mixner & Turner (1941) failed to induce in cyclic rats by periodic application of turpentine to the nipples, is explicable in the light of the modern conception of prolactin as a third gonadotrophin (luteotrophin) responsible for the maintenance of luteal function (for references to some of the papers which cite evidence in favour of this concept see Hisaw & Astwood, 1942; Parkes, 1944; Hooker, 1946) provided that one assumes

that the suckling-stimulus causes the release of prolactin by the hypophysis.

Related observations, such as those of McKeown & Zuckerman (1938), who found that destruction of the corpora lutea of lactating rats was not followed by oestrus, provided that suckling was continued, and of Desclin & Grégoire (1937), who observed luteinization of ovaries implanted into rats spayed at parturition, again only in the presence of suckling, while they are not necessarily concerned with prolactin secretion do add to the evidence that suckling can profoundly modify the secretion of hormones by the anterior hypophysis. A similar conclusion follows from the results of Desclin (1947), who found that suckling prevented the appearance of "castration cells" in the hypophyses of rats spayed at parturition and subjected to ligation of the galactophores, and of Grégoire (1947a) who found that gestational involution of the thymus was to some extent maintained in spayed parturient rats with galactophores cut, provided that suckling was maintained. Since in neither case could the effects of suckling be simulated by prolactin administration (Desclin, 1947; Grégoire, 1947b), it would appear that nervous control of other anterior-pituitary functions—secretion of follicle-stimulating hormone and adrenotrophin respectively—was involved.

Though, as we have seen, there is considerable circumstantial evidence in favour of the existence of a neurohormonal mechanism responsible for the maintenance and perhaps the initiation of lactation, we are on much less sure ground when we come to the question of the neural pathways involved. The sensory nervous pathway from the mammary glands to the higher centres of the central nervous system is not difficult to visualize in broad outline, but the terminal links in the pathway from the hypothalamus to the adenohypophysis are far from clarified. While the existence of nerve-fibres passing from the hypothalamus to the pars nervosa is fully established, the evidence for similar fibres extending from the pituitary stalk into the pars distalis is still conflicting (e.g. see Green & Harris, 1947). In this connexion, recent experiments on the effect on lactation of section of the pituitary stalk are of obvious interest, but unfortunately the available evidence is far from unanimous. On the one hand Herold (1939) and Desclin (1940) reported that the young of lactating rats which underwent stalk-transection died despite vigorous suckling, and concluded that the production of lactogenic hormones was maintained by impulses from the diencephalon passing through the infundibular stalk. On the other, Dempsey & Uotila (1940) found stalk-transection to be without effect on lactation in the same species, a result in agreement with one case in the human reported by Dandy (1940). A later paper by Jacobsohn & Westman (1945) reports results which are at first sight somewhat intermediate between these two points of view, in that, though pituitary-stalk transection in lactating rats was followed by considerable mammary involution and the sucklings died, the involution was, however, not so complete as after weaning or hypophysectomy. They therefore seem disinclined to accept the interpretation of Herold and Desclin. Jacobsohn & Westman point out that stalk-transection inevitably involves considerable interference with the blood-supply of the pituitary, which might result in temporarily-diminished secretion of the anterior-pituitary hormones necessary for the maintenance of lactation, and hence in temporary failure of lactation until the re-establishment of an adequate hypophyseal circulation. By this time, however, it might well be that the young are past saving, and considerable areas of the mammae irreparably involuted, so that functional response to anterior-lobe hormones is no longer possible. In areas in which involution is less advanced secretion might ultimately become re-established, as Jacobsohn & Westman suggest. Herold and Desclin performed their operations after parturition, just as did Jacobsohn & Westman in some cases, so that operational damage to the pituitary might well have been a factor. Desclin, however, reported the presence of functional anterior-lobe tissue in those of his animals in which stalk-transection—as revealed by subsequent histological examination—was complete and which failed to rear their young. Moreover, he found that in cases where the operation subsequently proved to be incomplete the young were reared, and such cases might be considered as providing the control operations which the other investigators omitted. In the experiments of Dempsey & Uotila, a considerable time was allowed for recovery from the effects of the operation before the rats were mated, so that some sort of hypophyseal circulation might well have been re-established, but the lactational data, as given, are hardly sufficient to allow of the conclusion that lactation was normal.

The results of the experiments on pituitary-stalk transection thus contribute very little to the elucidation of the question of the mechanism governing prolactin secretion. In any event it must be remembered, just as in the case of the results of Ingelbrecht (1935), that even if it were proved that stalk-transection interferes with lactation, the result would not necessarily be relevant to the truth or otherwise of the theory of Selye, since the observed lactational failure might equally well be due to destruction of the mechanism governing milk-discharge, in which nervous impulses passing through the pituitary stalk are also probably involved (see below).

Incidentally, in the present connexion it may be well to remember that there is good reason for the belief that in forms such as the rabbit, which do not ovulate spontaneously, it is probable that the activity of the anterior hypophysis is stimulated by a reflex pathway involving the hypothalamus and the infundibular stem. Another possibility that should be considered, however, is that the anterior lobe may be stimulated humorally by an agent reflexly secreted by the neurohypophysis and passing to the adenohypophysis by the portal vessels (see Green & Harris, 1947).

One further point regarding the possible effect of the suckling-stimulus on milk-secretion must be borne in mind. Since there is considerable evidence (see Folley[1], 1947; Young[2], 1947) that a complex of anterior-lobe hormones, rather than prolactin alone, is responsible for the maintenance of lactation, if a neurohormonal reflex of the kind postulated by Selye does operate to maintain lactation it must almost certainly cause the discharge by the anterior lobe of other hormones besides prolactin.

Though the removal of the suckling-stimulus is undoubtedly an important factor in bringing about mammary involution after weaning, it seems probable that the effects of non-removal of milk also make some contribution.

[1] [*BMB* 1101]
[2] [*BMB* 1104]

Selye & McKeown (1934c) found that while lactation in mice may be prolonged for more than two months by the repeated fostering of actively-suckling litters, involution (of a histologically abnormal type) does eventually occur. Moreover it should not be forgotten that Kuramitsu & Loeb (1921) and Hammond (Hammond & Marshall, 1925) had many years previously reported involution in glands, the suckling of which was prevented by occlusion of the nipples with collodion, despite the continuation of suckling at other glands in the same animal (see also Fauvet, 1941). Some other cause than the two just mentioned must be postulated to account for the gradual involution which occurs in the mammae of milk-producing ruminants despite regular application of the milking-stimulus always accompanied by withdrawal of milk.

3. Discharge or Withdrawal of Milk from the Mammary Gland: Physiology of Milking

The process of obtaining the full yield of pre-formed milk from the mammary gland by suckling, or in the case of domesticated milk-producing animals such as the cow and goat by artificial hand- or machine-milking, involves far more than evoking mere relaxation of the teat-sphincter and the removal of milk by rhythmic compression of the teat (and perhaps, in the case of the human, the lactiferous sinuses) and gentle suction. It is a psycho-physiological complex, the details of which are only now in the process of being elucidated. Of necessity, most of the existing information has been obtained from investigations on the cow, and to a lesser extent the goat, and the present discussion will thus be centred on the physiology of milk-discharge as it applies to milking of the cow. It seems likely, however, that similar considerations will apply to other animals; a recent clinical contribution by Waller (1943) certainly suggests that they apply to suckling in woman.

The main facts governing the milking-process in the cow are summarized in their essentials in this paragraph. They exist as scattered observations in the literature, often published in rather obscure journals, but happily many of them have been succinctly reviewed and collated by Hammond (1936) in a valuable article to which the reader is referred for references to the original papers; lactational physiologists are indebted to J. Hammond for this able appreciation of the diffuse literature of a rather obscure field. The mammary gland of the cow or goat is provided with a cistern or system of cisterns which, together with the larger ducts, are capable of storing a certain amount of milk between milkings. This, however, amounts to a relatively small proportion of the milk present in the udder at milking-time, most of which is tenaciously held, presumably by capillary forces, in the lumina of the alveoli and in ducts of very fine calibre. If a teat is cannulated in such a way as to avoid sensory stimulation of this or other teats (incidentally this would seem, from the work of Gaines, 1915, to be far from easy), only the milk present in the cisterns and larger ducts can be so removed; the full yield of milk from the cannulated gland can be obtained only when its own or another teat in the same animal is properly palpated, or any other milking-stimulus, to which the animal is conditioned, is applied. In the normal course of events, the application of the suckling- or milking-stimulus is followed, after a brief interval, by a sudden rise in milk-pressure within the udder—the so-called "let-down"—only after which can the full yield be obtained.

Hammond (1936) has drawn attention to much evidence, existing in the literature, which effectively disposes of the fallacious idea, once widely held and surprisingly persistent, which ascribed the pressure-increase to reflex secretion of milk. This and other evidence he put forward in support of the theory that the "let-down" is due to a nervous reflex, initiated by stimulation of the teat, as a result of which the milk is squeezed down from the alveoli and finer ducts into the larger ducts and cisterns, from which it readily flows during milking. It was held that this reflex can be conditioned to sensory stimuli associated with the normal routine of preparation for milking, and can be inhibited by impulses from the brain arising from unfavourable stimuli such as sudden noises or the approach of an unfamiliar milker. The idea that the "let-down" is due to a nervous reflex was, of course, not new; for instance Gaines (1915) believed that it was caused by reflex contraction of smooth-muscle fibres in the mammary tissues in response to stimuli normally associated with suckling. Hammond, too, postulated a purely nervous arc, but conceived the terminal stage as involving a state of "erection" of the udder tissues, efferent impulses from a centre in the cord being supposed to cause contraction of smooth-muscle fibres running in conjunction with or over the venous vessels of the udder, thus occluding them and engorging the udder-tissues with blood. Hammond suggested that the mechanism of udder "erection" was somewhat similar to that involved in erection of the penis; if this were so, it would of course be necessary to assume the occurrence of *relaxation* of the tonus of the smooth muscles in the walls of the arterial vessels of the udder. Hammond also considered the possibility that the reflex contraction of myo-epithelial cells (basket cells) surrounding the alveoli might be involved in the "let-down", but the existence of myo-epithelial cells in close connexion with the alveolar epithelium, at any rate in decisive numbers, has never yet been conclusively demonstrated (but see Swanson & Turner, 1941), neither has anyone yet seen a myo-epithelial cell, in the mammary gland or elsewhere, contract (see Richardson, 1947)[3]. The contractile properties of myo-epithelial cells have been assumed only by analogy with the structural appearances of smooth-muscle cells.

In recent years this theory has had to contend with a rival which postulates a neurohormonal mechanism as responsible for the "let-down", the centripetal portion of which is purely neural while the centrifugal portion involves a hormonal phase. This theory developed from the undoubted fact (see accompanying article[4] by Folley, 1947) that injection of posterior-lobe extract evokes in the mammary gland a condition resembling the "let-down", in that its administration to a lactating animal causes a sudden increase in the milk-pressure, presumably due to a "contractile process" involving smooth-muscle fibres or other cells with similar properties in the mammary tissues, thus forcing the milk from the alveolar tissues and favouring its ejection or withdrawal from the gland. The neurohormonal theory holds that stimulation of the teat or other conditioned stimulus causes reflex secretion of the oxytocic

[3] [*BMB* 1099]
[4] [*BMB* 1101]

principle by the posterior pituitary, which in turn, by evoking the contraction of smooth-muscle tissue in the mammary gland, is directly responsible for the "let-down".

Many years ago, Gaines (1915) described interesting experiments which, as we can recognize today, strongly suggested a physiological role for the posterior pituitary in normal suckling or in the milking-process. Perhaps the most cogent of these for the point under discussion was the demonstration that, while anaesthesia inhibited the "let-down" in a bitch, so that the pups suckled in vain, they were able to satisfy their hunger shortly after the anaesthetized mother received an injection of posterior-pituitary extract. Gaines, however, did not specifically postulate a physiological role for the posterior lobe in the suckling- or milking-process, though he drew attention to the similarity between the effects on the mammary gland of the nursing-stimulus and those of posterior-pituitary extract, and it remained for Ely & Petersen (1941), on the basis of experiments in which *inter alia* they showed that, in cows in which the motor nerve-fibres to one half of the udder had been severed, the "let-down" could be evoked by oxytocin or alternatively inhibited by fright or injections of adrenalin in both halves of the udder alike, to postulate what seems, in the light of present knowledge, perhaps the most plausible theory of the mechanism of milk-discharge yet advanced—a theory which incorporated the idea that the ejection of milk from the udder depends on a balance between circulating oxytocin and adrenalin. Incidentally, in connexion with these experiments of Ely & Petersen on nerve-section, the possibility of the regeneration of inguinal nerve-fibres during the two months which elapsed between the operation and the experimental observations, was pointed out by Espe (1947), but it seems likely that this possibility is remote. Further evidence that the agent directly responsible for the "let-down" was hormonal in nature was later reported by Petersen & Ludwick (1942), who state that addition of blood from a cow in which the "let-down" had been induced in the usual way, to the fluid perfused through an isolated udder, caused the ejection of milk from the latter, while blood from an unstimulated cow was without effect. These experiments have so far been reported only in a short abstract; in view of their interest, it is a pity that a definitive publication has not appeared.

Much of the evidence which can be adduced in favour of the neurohormonal theory of milk-discharge, just outlined, is obviously circumstantial, and much further work remains to be done before the analysis of the complex of events involved in the efficient removal of milk from the mammary gland during natural suckling or artificial milking can be considered as anywhere near complete. Thus, it cannot be taken as fully established that the oxytocic principle of the posterior lobe is the effective agent in evoking the "let-down". Turner & Cooper (1941), who attempted to devise a method of assay for what, for want of a more elegant term, might be called mammary-gland "let-down" activity, found that posterior-lobe extracts rich in pitressin were more active than would be anticipated from their oxytocin content. Their results appeared to indicate either that the effect might be due to the combined action of oxytocic and pressor factors, or to a third factor present in both types of posterior-pituitary extract. The possibility that the "let-down" might be due, at any rate in part, to a vasomotor action of the type postulated by Hammond (1936), but evoked humorally, must therefore be considered.

In addition, there are other and more serious uncertainties regarding the means by which the increase in milk-pressure is achieved. Ely & Petersen (1941), and Swanson & Turner (1941) speak respectively of the contraction of "musculature" or "muscle fibres" surrounding the alveoli, and the latter claim to have demonstrated "the presence of cells beneath the secretory epithelium of the alveoli and in the interlobular spaces which had the appearance and staining properties of smooth muscle fibres". Nevertheless, in the writer's opinion there is no satisfactory evidence yet available of the existence of smooth-muscle fibres in close association with the mammary alveoli. If these authors are referring to myo-epithelial cells (the so-called basket cells), it may once more be repeated that the existence of these rather elusive elements close to the alveolar epithelium, at any rate in numbers sufficient to account for the observed increase in milk-pressure, requires further confirmation, and in any event their contractile properties in response to oxytocin or to any other stimulus have still to be demonstrated (on these points see Richardson, 1947)[3].

Notwithstanding these uncertainties, it seems fair to conclude by saying that recent work on the physiology of the milking-process has reached a stage of considerable interest from the practical aspect, if for no other reason than because of the attention it has inevitably focussed on the importance of the suckling- or milking-process as a component of the total phenomenon of lactation. As pointed out above, a failure of the milk-withdrawal mechanism will amount to a failure of lactation (see for example Gomez, 1939, 1940), and habitual failure to remove all the available milk because of some inherent defect in the discharge-mechanism, or, in the case of a cow, because of faulty milking-technique, may well react unfavourably on the secretory process in such a way as to lead to a shortening of the lactation-period. A certain amount of rather indirect experimental support for this concept has been provided by Miller & Petersen (1941) and Knodt & Petersen (1944). All will agree that more decisive experiments will be welcome.

Waller (1943) claims to have obtained evidence in support of the reasonable belief that a mechanism of the type discussed above, governing the discharge of milk, exists in women (see also Waller, 1947a, 1947b[5]). It is evident that psychological and neural factors must be of especial importance in man, and many cases of partial or complete lactational failure in parturient women may well be due to breakdown of the reflex mechanism called into operation by suckling.

The foregoing discussion should serve to emphasize that the physiological phenomenon which in agricultural circles has often been known as the "let-down" or "letting-down" of milk, and in medical circles as the "draught", is an *active* process. The make-shift term "let-down", used in this review for want of a better, is thus hardly appropriate, connoting as it does rather the release of some restraint on the flow of milk which otherwise would flow freely from the alveolar tissues, than an active and forceful expression of milk therefrom. Even more is it inappropriate to describe the situation in which the "let-down"

fails to occur, in traditional terms of the cow "holding-up" her milk. Quite apart from the fact that this may be held to imply some conscious act on the part of the animal, for which there is no evidence, it also carries the inacceptable suggestion that the egress of milk from the alveolar tissues is actively prevented. Clearly, more precise terminology is required in this field.

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BIOCHEMISTRY OF MILK-SECRETION

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The immense biological advantage that mammals have derived from the continued postpartum relationship between mother and offspring involved in the process of lactation is obviously associated with deep-seated, specialized developments of form and function in the mammalian female—anatomical and histological, physiological and biochemical. In this article it is the last of these that will receive the main attention, though clearly the biochemistry of milk-secretion cannot be dealt with entirely *in vacuo*; the gross and the minute structure of the mammary gland, nutrition and the storage of nutrients in the body, general metabolism, the endocrine control of mammary growth and function, are all closely involved.

I shall begin by stating briefly the findings which are now generally accepted as reasonably certain regarding the wider biochemical aspect of milk secretion and shall then discuss critically methods and results of fairly recent experimentation in this field.

a. It is quite obvious that all the constituents of the milk must be carried, in some form or another—not of course necessarily in the form in which they occur in milk—by the blood to the mammary gland, and there taken out of the blood and appropriately modified. Like blood-plasma, milk contains, in addition to characteristic constituents in easily measurable quantities, a large assortment, in smaller amounts or only in traces, of the biologically-important organic and mineral compounds present in the animal body. The peculiarly characteristic milk-constituents, casein, lactose and milk-fat, do not occur as such elsewhere in nature, whilst citric acid, calcium, potassium, inorganic phosphate, vitamin A, vitamin B_1, riboflavin, nicotinic acid and vitamin C are found in considerably greater concentration in milk than in blood-plasma. The mammary gland, therefore, is capable both of synthesis and of concentration (see table I).

TABLE I. IMPORTANT CONSTITUENTS OF BLOOD-PLASMA AND MILK

	Blood (plasma) constituents	Milk-constituents
Nitrogenous ...	albumin globulin *glycoprotein (a globulin) (?*) amino-acids urea	‖casein ‖lactalbumin ‖lactoglobulin amino-acids urea
"Fatty"	*blood-fat phospholipin cholesterol and cholesterol esters	‖butter-fat phospholipin cholesterol and cholesterol esters
"Carbohydrate" etc.	*glucose lactic acid pyruvic acid *β-hydroxybutyric acid	‖lactose traces of glucose ‖citric acid
"Mineral"	*inorganic phosphate phosphoric esters potassium sodium *calcium chloride	§inorganic phosphate §phosphoric esters §potassium †sodium §calcium †chloride
Other constituents	vitamin A and carotene vitamin B_1 and several members of this group vitamin C	§vitamin A and carotene §vitamin B_1 and several members of this group §vitamin C

* known to diminish in percentage in blood in traversing the mammary gland
† diluted in milk as compared with blood-plasma
§ concentrated in milk as compared with blood-plasma
‖ characteristic milk-constituents

b. Milk-secretion usually takes place fairly continuously over the whole of the 24 hours of the day. Nevertheless, with an actively-lactating animal, secretion may be so rapid as to fill up and distend the storage-spaces of the gland in a very few hours to such a degree that, if suckling or milking does not take place, further milk-secretion is inhibited and, at least in the dairy cow, preferential resorption of some of the milk constituents, e.g. the fat, may take place.

c. There is a quantitatively large and continuous utilization of oxygen by the lactating gland. As is obvious from the very large blood-flow (mentioned again later) through this gland, and from the definitely venous character of the out-flowing blood, some carbon compound or compounds must be undergoing oxidation at a considerable speed.

d. Milk has, within very narrow limits, the same osmotic pressure as blood. This is to be expected, as a characteristic of an intra-cellular secretion (see later) which remains for some time in most intimate contact with the cytoplasm before it is discharged from the cell.

c. It is generally accepted that *all* the constituents of the milk are secreted by one type of cell, the large cuboid cells with big nuclei which line each alveolus of the mammary gland. These milk-secreting cells, attached to a basement-membrane, are fairly permanent structures; milk does *not* (as was once surmised) originate from the breakdown and dissolution of complete cells which are entirely renewed, time after time, from the basement-membrane. If this were so, there would be far more mitosis and cellular repair during lactation than can be observed histologically, and there would also be much larger quantities of substances in the milk derived from cell nuclei. In fact, nucleoproteins and their breakdown products are present in normal milk in no more than traces. Milk must be regarded as an extruded, intra-cellular secretion, containing at most only small quantities of cytoplasmic, and practically no nuclear, material. Milk however varies so greatly in composition from one species to another[1] and to a lesser extent in the same animal at different times, that there must be a marked difference in the quantitative make-up of the secreting mechanism in the alveolar cells of different species, and probably also in the detailed hormonal control of that mechanism.

For present purposes the biochemistry of milk secretion may be regarded as beginning with the preparation of the gestating animal for lactation. The maternal organism has not only to meet the demands of the growing foetus, but at the same time to accumulate reserve materials for efficient lactation. A common dairy-farm practice is the "steaming-up" of a heifer or cow during the last few weeks before calving, by feeding extra concentrates, which in addition to calories should contain "digestible protein", carotene and minerals. By this means additional nutrients are stored in the pregnant animal and it has been demonstrated (Blaxter, 1944, amongst others) that increased yields of milk may be obtained in the subsequent lactation without the loss of condition of the cow which otherwise not infrequently follows if she has been inadequately fed during late gestation. The hypertrophied uterus also serves during involution as a source of nitrogen which is partially, at least, made available for synthesis of milk proteins. It has been clearly shown that the cow stores calcium and phosphorus in the skeleton during pregnancy, for release during lactation (Forbes *et al.* 1935). Warnock & Duckworth (1944) have demonstrated that in rats calcium and phosphorus are stored during gestation in the "ends" of the long bones, and that demineralization occurs in the "ends", but not to a measurable extent in the shafts, during lactation.

In the colostrum is "stored", in addition to globulin with its associated antibodies, vitamin A, and in some animals relatively large quantities of vitamin C.

The possible biochemical transformations which take place during milk-secretion will now be considered more closely. In table I is a list of some of the quantitatively more important constituents of blood-plasma and of milk. Only *plasma* constituents are given, since while it cannot be completely ruled out that the erythrocyte, in squeezing through a narrow capillary, might exchange more than oxygen and CO_2 with the surrounding tissue, there is so far no definite evidence that this cell plays a direct part in the carriage of nutrients to the mammary gland.

[1] The milk of the porpoise, or whale (the offspring of which have to put on a fatty blanket as soon as possible) contains over 40 % of fat (Davies, 1939) whilst that of the mare contains about 1 %. The milk of the rabbit, whose offspring grows with great rapidity, doubling its birth-weight in 6 days, contains 10 % to 15 % of protein, and some 2.5 % of minerals, whilst that of the woman, whose offspring grows at a more leisurely rate, contains about $^1/_8$ that amount of protein, and $^1/_{10}$ that amount of minerals.

A. EXPERIMENTAL METHODS

1. Arterio-Venous Changes in Blood-Composition (A-V Method) in the Unanaesthetized Animal

The obvious way to determine what blood-constituents are taken up by any tissue for purposes of synthesis of new materials, maintenance of tissue-structure, or for the production of energy is directly to compare the composition of the blood entering, with that of the blood leaving, the tissue. This method, which is one of some experimental difficulty, has been used in the case of the mammary gland for fifteen years or more, usually with the cow or the goat, but has so far yielded somewhat disappointing results.

Arterial blood is taken from any convenient vessel in the arterial system—an accessible artery in the cow is the internal iliac artery, approached through the rectal wall (Graham, Kay & McIntosh, 1936)—and, as nearly as possible simultaneously, venous blood is taken from the easily-accessible abdominal (subcutaneous) mammary vein. Between this vein and the smaller veins draining the udder there are anastomoses, so that a sample from this vein may be taken as a fair sample of the true venous outflow. The venous sample is in practice taken a few seconds *before*, and never after, the arterial sample. It was clearly shown some years ago by the same workers that the cow is extremely sensitive to disturbance, and may react to it by rapid changes in the composition of the blood which are often sufficient to destroy the significance of any conclusions, based on arterio-venous differences, regarding the precursors in blood of the milk-constituents.

2. Arterio-Venous Changes in the Anaesthetized Animal

To avoid the uncertain results obtained by some of the earlier investigators who did not fully realize that excitement in the animal when blood-samples are being taken tends to invalidate A-V analyses, several experiments have of recent years been carried out on the anaesthetized animal (cow or goat), using nembutal (Reineke, Williamson & Turner, 1941; Reineke, Stonecipher & Turner, 1941; Shaw, 1946). These workers have shown that milk of normal composition continues to be secreted at normal rates by animals anaesthetized in this way.

An uncertainty, the importance of which it is not yet possible to assess, but which applies equally to the normal and the anaesthetized animal, is associated with the fact that in addition to milk and to venous blood, there is also a drainage of *lymph* from the secreting mammary gland. As to the composition of mammary lympha, little is known, though Shaw & Petersen (1940) say that it contains some calcium, but little fat. As to volume, there can be no doubt, in view of the capacious and elaborate system of lymph-vessels present in mammary tissue (El Hagri, 1945), and from general observations, that the flow of lymph in the lactating gland cannot be negligible. Whilst its volume may be small relative to that of the venous outflow, it may

well be greater than that of the milk secreted in a given time. This awkward problem has not yet been adequately faced by those using the A-V method of studying the biochemistry of milk-secretion. Whilst it may well be that mammary lymph-flow is of little quantitative importance in drawing up the balance sheet between glandular intake and output, we shall be handicapped in arriving at any clear conclusions regarding the precursors in the blood of the milk-constituents until the composition and rate of flow of mammary lymph are considerably better known.

3. The Isolated Perfused Mammary Gland

To surmount some of the experimental difficulties of the A-V method in the intact animal, Petersen, Shaw & Visscher (1941) developed a technique whereby the udder of a normal, lactating cow was rapidly excised and immediately, i.e. within 7–8 minutes, perfused with warm oxygenated (defibrinated or heparinized) blood. Milk-production continues and the uptake of "precursors" from the circulating blood remains similar to that found in a normal, intact gland. By thus eliminating the cow, the distorting effect of excitement is also eliminated. Various substances suspected of being concerned in milk-production can be added to the blood, the rate of blood-flow can be accurately measured, and samples of "arterial" and "venous" blood can be taken at any intervals with great ease. The technique is clearly one that requires no little experimental skill.

In the sense that it does not circulate through the body and tap the various storage-depots, nor receive endocrine secretions, the blood used for perfusion soon ceases to be strictly arterial. The question also as to how far interference with lymphatic drainage affects the findings remains an open one. The isolated gland deteriorates fairly quickly—within some six hours. Moreover, whilst most recent observers have found respiratory quotients of above 1 (usually 1.1 to 1.3) for the normal functional mammary gland in the intact animal, the isolated perfused gland gives a value (Shaw, 1939) of 0.8.

4. Mammary-Gland Slices

The method of incubation, in well-oxygenated salt-solutions, of fresh slices of mammary tissue with various possible precursors of milk-constituents was first used by Grant (1935). It has recently been further developed by Knodt & Petersen (1945, 1946a), and has obvious possibilities for the future.

Mammary slices suspended in saline are, of course, very different from the intact lactating gland, but investigation of the biochemical processes which occur in such slices may at least give an indication of the synthetic and metabolic potentialities of the same tissue under more strictly physiological conditions.

5. Use of Isotopes

This very promising method has so far been very little used in relation to mammary secretion, either with radioactive isotopes, or with "heavy" elements such as deuterium. Earlier work of Aten & Hevesy (1938) was interrupted by the war, and later experiments of Erf (1941), Erf & Pecher (1941), Pecher & Pecher (1941) and McConnell (1942) have not yet proceeded very far. The use of isotopes such as ^{13}C has recently provided information, which may have considerable bearing on the biochemistry of mammary secretion, on possible paths in the intermediary metabolism of carbohydrates and fats in liver- and kidney-tissue.

6. Effect of Diet and Hormones on Milk-Composition

The study of the effect in the lactating animal of inanition (Smith & Dastur, 1938) or of feeding special diets (Hilditch & Paul, 1936; Hilditch & Longenecker, 1938; Hilditch & Jasperson, 1941, 1943) or of treatment with hormones[2] such as thyroxin (Folley & White, 1936; Smith & Dastur, 1940), oxytocin (Shaw, 1942), anterior-pituitary hormones (Folley & Young, 1938; 1939), oestrogenic hormones (Folley, Watson & Bottomley, 1941), insulin (Gowan & Tobey, 1931) on the detailed composition of the milk has also thrown some indirect light on the biochemical transformations during lactation.

7. Direct Biochemical Examinations of Mammary-Gland Tissue

By the determination, under different physiological conditions, of tissue constituents such as glycogen (Petersen & Shaw, 1938; Knodt & Petersen, 1946b) and by direct or indirect examination of the enzymic function of the gland (Folley & Kay, 1935, 1936; Folley & Greenbaum, in press), data have been obtained which, by cautious fitting in to the puzzle, add a little more to our slowly-developing picture of mammary secretion.

B. FINDINGS

In this section an attempt will be made to summarize and interpret the data obtained by the different methods of investigation just described. As in other sections, it will not be possible to cite here more than a few of the contributors to these data.

8. General

The following constituents of the blood-plasma fall in concentration in passing through the mammary gland:—blood-sugar, inorganic phosphate, "neutral fat", (Graham, Jones & Kay, 1936; Voris, Ellis & Maynard, 1940; Shaw & Petersen, 1940), calcium (Shaw, Powell & Knodt, 1942), β-hydroxybutyric acid (Shaw & Knodt, 1941), amino-acids (Blackwood, 1932; Graham, Peterson, Houchin & Turner, 1938; and more recent workers), one of the plasma globulins and glycoprotein (Reineke *et al.* 1941), oxygen (as oxyhaemoglobin).

The following remain without detectable change:—phospholipins, cholesterol (Graham *et al.* 1936), haemoglobin, cell-volume, pyruvic acid (Shaw, 1946). There is still some doubt as to whether there is any significant change in the concentration of lactic acid, some workers finding a diminution (Graham, 1937; Boyd & Petersen, 1938), others no change (Powell & Shaw, 1942).

As might be expected with any active tissue, there is much more CO_2 in the mammary venous than in the arterial

[2] [See also *BMB* 1104.—Ed.]

blood. There also appears to be more urea (Graham, Houchin & Turner, 1937) in the venous blood.

9. Rate of Blood-Flow through Mammary Gland

The very rapid rate of blood-flow, inferred by Graham *et al.* (1936) for the cow, on the basis of the ratio of A-V changes in probable precursors to the concentration of the milk-constituents produced in the secreted milk, to be of the order of 400-500 volumes of blood per volume of milk secreted (i.e. for a good cow some 6 to 7 litres per minute), has been confirmed, by a better method based on calcium- and phosphorus-uptake from blood, by Shaw *et al.* (1942).

10. Respiratory Quotient

As regards the gaseous exchange, there is general agreement that, in a given interval of time, a greater volume of CO_2 is produced by the secreting gland than the volume of oxygen used by it (Graham, Houchin, Peterson & Turner, 1938; Reineke *et al.* 1941; Petersen & Shaw, 1942; Bottomley, unpublished experiments; Shaw, 1946; and several other workers). That a respiratory quotient exceeding 1, usually between 1.1 and 1.3, is to be found for both cows' and goats' mammary glands when the animals are normally fed, and not agitated, must be accepted as true. The classical conclusion from this would be that fat is being formed from carbohydrate but, as will be seen, this conclusion is open to doubt.

The gland of the fasting, lactating cow appears to give a respiratory quotient of below 1 (0.88, according to Shaw, 1946).

11. Lactose

There is little if any glucose in normal milk. The amount of glucose that disappears from arterial blood in traversing the mammary gland, which may be as great as 25 % or even 30 % of the total arterial blood-sugar, is about sufficient to account for the whole of the lactose. Grant (1935) showed that mammary-gland slices would synthesize lactose if incubated with a solution of glucose, but were not apparently able to do so from fructose, mannose, galactose, or various carbohydrate phosphoric esters. Knodt & Petersen (1943) have confirmed this synthesis, and shown that glucose + lactic acid, maltose and glycogen also give lactose under similar conditions. Gowan & Tobey some years ago (1931) in experiments on the effects of inanition, of insulin and of phlorrhizin administration on the lactating cow, were the first to show that the quantity and percentage of lactose secreted in a given time are very sensitive to a lowering of the blood-sugar level, however this lowering is brought about. Their findings on the intact animal were confirmed by others, and similar results were obtained in the excised, perfused udder by Knodt & Petersen (1946b), who found that the addition of insulin to the perfusing blood causes a rapid drop in lactose-production in the gland. Glycogen, however, increased in quantity in the insulinized gland. These effects were found either with a normal blood-glucose, or when additional glucose was put into the perfusing blood.

The normal lactating gland contains some 0.2 % of glycogen (Petersen & Shaw, 1938), but the non-lactating gland very little. It may well be that glycogen is an intermediate stage between blood-glucose and milk-lactose.

The circumstantial evidence—and not all is quoted here—that lactose is derived from blood-glucose is thus very strong, but whether a part of the blood-glucose taken up is used for energy-purposes in the gland, or even for manufacturing some milk-constituents other than lactose, is by no means clear.

So many oxidizable carbon compounds in addition to glucose are taken up from the blood by mammary tissue (e.g. β-hydroxybutyric acid, glycoprotein, blood-fat and even amino-acids) that it is not yet possible to state with certainty which, if any, are actually consumed for energy-purposes in the gland. Shaw considers that β-hydroxybutyric acid is one of the principal substances so used. It seems to me conceivable, in fact likely, that, as in other tissues, *several* of the blood-constituents may be in equilibrium with glycogen or some other labile substance within the large alveolar cells, in such a way as to provide enough precursor both for lactose-secretion and for energy-purposes. Recent experimentation with ^{13}C and other isotopes has demonstrated that some of our earlier views as to the limits of interconvertibility, in the presence of the powerful enzymic systems in the more active tissues, of biologically important carbon compounds may have been too conservative.

12. Milk-Fat

There is sufficient neutral fat taken up from the arterial blood to account quantitatively for all the milk-fat secreted by the lactating gland, but when cows' milk-fat is examined in detail, it is found that some 30 % of the fatty acids belong to the short-chain C_4-C_{14} series, which do not appear to be present in the blood-fat. Milk-fat, therefore, could not be produced merely by concentrating the neutral fat of the blood; more-extensive biochemical changes are involved. Moreover, the question again arises as to what part, if any, of the absorbed blood-fat is used in the gland for energy-purposes? Is part of the milk-fat —say the lower fatty-acid part—synthesized from other sources than blood-fat, perhaps from carbohydrates or from β-hydroxybutyric acid (a possibility suggested by Shaw & Knodt, 1941)? This is at least not rendered less likely by the fact that the respiratory quotient of normal mammary tissue is greater than unity.

As a result of detailed analysis of milk-fat, Hilditch & Sleightholme (1931) suggested that the glycerides containing short-chain acids might be produced in the mammary gland by oxidation of the alkyl end of longer-chain fatty acids of oleo-glycerides without actual hydrolysis of the latter. Hilditch & Paul (1936) brought further evidence in favour of this inherently rather surprising suggestion (which was made before Kelly & Petersen (1939) showed that free fatty acid was present to a much greater extent in lactating than in dry mammary glands), and Smith & Dastur (1938) interpreted the results of their experiments on the effect of inanition on the distribution of fatty acids in milk-fat, in which they found that the content of short-chain fatty acids decreased markedly whilst there was a corresponding increase in oleic acid, as supporting Hilditch's views. The findings of previous observers that

the respiratory quotient of the mammary gland of the *fasting* cow is less than 1, were confirmed by Shaw, Powell & Knodt (1942), who examined the milk-fat secreted by cows with severe ketosis (ketonaemia with hypoglycaemia) accompanied by varying degrees of inanition. They showed that the proportion of short-chain fatty acids was, in this condition, much below normal, in spite of the large excess of β-hydroxybutyric acid in the circulating blood. They consider therefore that this substance is excluded as a possible source of the short-chain fatty acids. On feeding large quantities of glucose to cows with ketosis, the proportion of very-short-chain fatty acids increases.

One cannot avoid associating these findings, as well as those of Smith and Dastur just quoted, with the recent results from Barcroft's laboratory where it has been found (Barcroft, McAnally & Phillipson, 1944; McAnally & Phillipson, 1944; Elsden, Hitchcock, Marshall & Phillipson, 1945; Danielli, Hitchcock, Marshall & Phillipson, 1945) that the ruminant is able to take up short-chain fatty acids, resulting from the microbiological breakdown of carbohydrate in the rumen, direct through the rumen wall, and that these acids may circulate in the blood. On the other hand, unpublished preliminary experiments carried out by Malpress in 1940, in which relatively large quantities of sodium butyrate were fed to lactating ruminants, gave no detectable increase in the proportion of volatile fatty acids in the milk-fat.

In the case of human milk-fat, Hilditch & Meara (1944) have shown that there is no butyric and practically no C_6 or C_8 fatty acid present. There are about the same quantities of C_{10}, C_{12} and C_{14} acids as in cows' milk-fat. (They point out, incidentally, that in regard to its component acids, human milk-fat has far more resemblance to a typical fat-blend of margarine than to butter-fat!) Shaw and his colleagues have expressed the opinion that the percentage of lower fatty acids in cows' milk-fat is much more closely associated with food-intake than with the level of blood-glucose, of lactic acid or of acetone bodies, and the findings of Hilditch and Meara may perhaps be interpreted as giving support to the view that these lower fatty acids are in some way related to the *ruminant* digestion of carbohydrate.

It must be remembered that the modern high-yielding cow—and this applies also to the goat—is an animal with an abnormally hypertrophied mammary system, and that the demands of the udder both for energy and for the precursors of the milk-constituents may be so insistent that extraordinary biochemical changes, such as the oxidation of part of the long-chain fatty acids of blood-fat to produce energy, may take place. In the goat, these acids are of rather longer chain-length—more C_6, C_8, C_{10} and less C_4—than in the cow. But how to reconcile these suggestions with the experimental finding that the respiratory quotient of the normal (cow's) mammary gland is greater than unity, i.e. that there is synthesis in the gland of oxygen-poor from oxygen-rich carbon compounds, remains an unsolved problem.

The fat of cows' milk, as secreted, contains in solution in the fat-globules, but not in the aqueous phase of the milk, both vitamin A and its precursor, carotene. Two remarkable observations which may eventually throw light on milk-fat secretion, and for which any complete biochemical account of mammary secretion will have to find a place, have recently been made by Kon and his colleagues. The first (Kon, Mawson & Thompson, 1944) is that whilst the vitamin-A content of milk-fat is more or less independent of the *size* of the fat-globule, i.e. the large, medium and small fat-globules all contain approximately the same proportion of vitamin A, the same is not true for carotene, of which the proportion is greater the smaller the fat-globule, i.e. there is more carotene as the relative surface-area/volume of the fat-globule becomes greater. The second (Kon & Ganguly, unpublished experiments) is that whilst in milk vitamin A is present almost entirely in the ester form, it is present in blood almost entirely as the unesterified alcohol.

13. Casein and Lactalbumin

Of cows' milk-proteins, casein is present in by far the largest quantity, some 2.9 % of the weight of the milk, lactalbumin is present to the extent of about 0.4 %, and lactoglobulin to about 0.05 % to 0.1 %. The last was shown by Crowther & Raistrick in 1916 to be identical with one of the globulins of bovine blood, whereas lactalbumin is not present in the blood-stream. Less is known with certainty about the precursors of the first two milk-proteins than about those of lactose or of milk-fat, perhaps because the lymph-leakage, mentioned earlier, has even more serious consequences in disturbing the protein balance-sheet than it has for that of carbohydrate or fat.

It has been accepted for some time that the total amount of amino-acids taken up as such by the lactating gland is insufficient to account for more than a small fraction of the protein appearing in the milk. Suggestions had been made from time to time that one or other of the major proteins of the plasma, after suffering a structural change of some magnitude, but probably not undergoing complete hydrolysis and resynthesis in the mammary gland, is the chief source of the major milk-proteins, but the first real evidence of such an origin was provided in 1941 by Reineke, Williamson & Turner, who found that an appreciable quantity of one of the blood-globulins, a glycoprotein, the molecule of which is believed to contain some 9 % of a carbohydrate-complex of galactose, mannose and glucosamine, leaves the arterial blood in its passage through the gland. The carbohydrate moiety of this protein may be concerned either in lactose-production or as a source of energy, but the other 90 % of the molecule is regarded by these workers as the main source of the milk-proteins. In view of the peculiar amino-acid constitution of casein, it is clear that in this case there must be some molecular rearrangement of the globulin, accompanied by subtraction of certain amino-acids, probably followed by their oxidation. This may account for the finding that more urea is present in the mammary venous than in the arterial blood. The problem of casein-formation is rendered even more complex by the observation that casein is a mixture of proteins with slightly different properties and composition (Linderstrøm-Lang, 1929) and different molecular weights.

Casein is, of course, a phosphoprotein, whilst the glyco-protein, from which it may well be formed, is not. By the use of radio-active phosphorus, Aten & Hevesy (1938) have shown that the phosphorus organically combined in the casein molecule is provided from the inorganic phosphate of the circulating blood.

14. Citric Acid

Citric acid, present in blood only in traces, occurs to the extent of some 0.2 % in cows' milk. Of the solid constituents of milk which remain after the major ones—lactose, milk-fat and protein—have been subtracted, it therefore forms about one-third. It is of great biochemical interest, as either citrate (or isocitrate with which it is in equilibrium) is now believed to be concerned, in many tissues at least, in the intermediary metabolism of carbohydrate, of fatty acids and of amino-acids alike. Its presence in milk may indicate its central importance in the biochemical changes accompanying milk-secretion.

The percentage of citric acid in blood is so small and analytical methods for determining it in these quantities are so relatively imprecise, that it cannot be said whether or not it is taken up from the blood by the mammary gland. Recent work of Knodt & Petersen (1946a) indicates, however, that mammary-gland slices incubated at 37.5°C. for 6 hours in the presence of oxygen with various substances—glucose, pyruvic acid, glycogen, maltose, lactic acid—or to a lesser extent when incubated alone without any addition, produce readily-recognizable amounts of citric acid, the amounts being greatest with glucose, and least with lactic acid. In presence of added β-hydroxybutyric acid, very little additional citric acid is formed. When *large* quantities of citric acid are added to mammary slices, some of it disappears.

Isolated mammary-gland tissue, therefore, can synthesize citric acid from various sources. It would be of interest to know whether added fatty acids or amino-acids increase the amount of citric acid produced by mammary slices under these conditions.

* * *

If there is one lesson which seems to me to emerge from the results at present available on the biochemistry of milk-formation, particularly when regarded in the light of the fairly recent disclosure of a far greater extent of interconvertibility than was previously supposed between proteins, fats and carbohydrates and the products of their hydrolysis and oxidation in many active tissues, it is that there is almost certainly a much more labile equilibrium within the alveolar secreting cells between the various substances taken in from the blood-stream and the various constituents of the milk in process of formation in those cells. It may eventually prove to be somewhat of an absurdity to speak of *the* blood precursors of this or that milk-constituent, or *the* source of energy for mammary metabolism, since different precursors for the same milk-constituent or different materials for combustion within the gland for energy-purposes may be used at different times—or even several at the same time—by the lactating mammary gland, depending, if commercial jargon may be allowed, on the current supply-position.

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EXPERIMENTAL STIMULATION (GALACTOPOIESIS) OF LACTATION

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1 Action of anterior-pituitary extracts in declining lactation
2 Action of anterior-pituitary extract in virgin animals brought into milk by oestrogen treatment
3 Economics of anterior-pituitary galactopoiesis in cows in declining lactation
4 Nature of the galactopoietic factors of the anterior-pituitary gland
5 Activity of thyroid-active substances: iodoproteins
6 Relationship of galactopoiesis and other endocrine phenomena
References

Folley & Young (1940) proposed the term "galactopoietic" to describe the action of a hormone preparation which enhanced the yield of milk in an animal already lactating; a galactopoietic endocrine extract was not necessarily "lactogenic", that is to say, it was not necessarily capable of initiating the secretion of milk in a non-lactating animal. Bergman & Turner (1940) independently suggested that the term "galactopoetic" or "galactogogue" be used for substances which augment established lactation. In the present review the terms "galactopoiesis" and "galactopoietic" connote ability to enhance established lactation without reference to ability to initiate milk-production.

This review is confined to the galactopoietic action of hormonal preparations in farm-animals, and will be largely concerned with the development of researches carried out in Britain during the war with a view to determining whether or not the large-scale employment of hormone preparations could lead to a significant increase in the country's total milk-supply.

1. Action of Anterior-pituitary Extracts in Declining Lactation

The demonstration by Stricker & Grueter (1928) and by Corner (1930) that anterior-pituitary extracts could initiate the flow of milk in suitable animals in the laboratory paved the way for the investigation of methods of augmenting the milk-yield of farm-animals on a large scale, but it was not until the results of the experiments of Asimov and his collaborators in the USSR had been published (Asimov, Kruze, Skaržinskaja, Mahova & Fominskaja, 1936; Asimov & Krouze, 1937) that the particular galactopoietic efficacy of a *crude* anterior-pituitary extract in cows in declining lactation was demonstrated. The experiments of the russian workers involved a single subcutaneous injection of a crude alkaline extract of ox anterior-pituitary tissue into a group of more than 500 cows in declining lactation. Such simple treatment induced substantial temporary increase in the milk-yield, the composition of the milk remaining normal. According to the investigators, the extra milk resulting from their experiments was produced at a financial profit. In the meantime, experiments involving the daily injection of large doses of prolactin (the so-called lactogenic hormone of the anterior pituitary gland) into goats, (Asdell, Brooks, Salisbury & Seidenstein, 1936) or cows (Folley & Young, 1937, 1938) in declining lactation had demonstrated that a substantial increase in milk-yield could thus be obtained, but the expense of preparing prolactin from the crude pituitary extract, together with the relatively low galactopoietic efficacy of crude prolactin, precluded the use of such treatment as a practical, profit-bearing process.

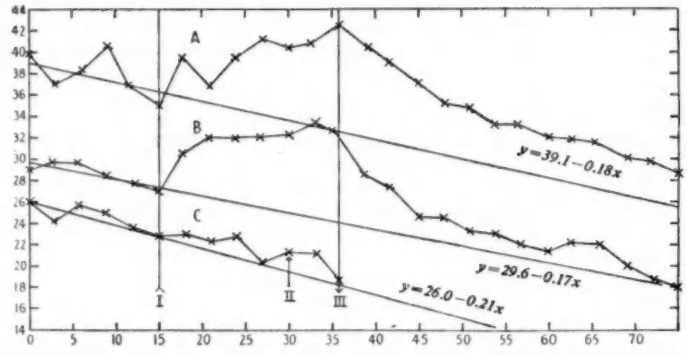
In an extensive investigation of the influence of treatment with various fractions of ox anterior-pituitary tissue on cows in declining lactation, Folley & Young (1938) agreed with Asimov *et al.* in finding that a single subcutaneous injection of a crude ox anterior-pituitary extract induced a substantial rise of milk-yield over a period of 5-6 days immediately after the injection, the mean increase in yield over this period being about 10 %. Even with the high cost of ox anterior-pituitary gland obtained for experimental purposes, the whole transaction was financially profitable to the extent that the sale of the extra milk yielded a sum about 33 % in excess of the cost of the glands.

Although any substantial increase in milk-yield must, in good husbandry, be accompanied by an increase in the food-supply to the animal, the basal cost of maintaining a cow, whether in milk or not, is so relatively large that the cost of the extra food required to cover an increase in milk-yield induced experimentally is always small in relation to the value of the extra milk. Accordingly, any procedure inducing an increased yield of milk in a milking animal is likely to be profitable provided that the cost of the treatment is not excessive, and it was clear from the early experiments of Asimov and his colleagues, and of Folley & Young, that pituitary treatment might provide an important and effective method of increasing milk-production on a large scale. This was of especial importance when, as was the case during and even before the war, it was desirable to increase the consumption of fresh milk by the population as a whole. Nevertheless, before the war no official interest was shown in Britain in the practical possibilities implicit in the hormonal treatment of cows in declining lactation, and the relevant researches followed conventional academic lines.

In a development of their earlier experiments, Folley & Young (1939, 1940) found that repeated injections of crude ox anterior-pituitary extract, given on alternate days over a period of about three weeks, raised the daily milk-yield of cows in declining lactation to an average level 15-20 % above that expected, from control data, in the absence of treatment. Moreover there was some indication in these experiments that, as the result of treatment lasting only three weeks, the whole level of milk-yield had been raised permanently, so that the curve of decline was parallel to, but above that, to be expected had the treatment not been given (fig. 1).

In all these experiments the quality of the milk, as revealed by analysis, was unimpaired, despite the substantial increases in yield; in fact, the only significant change in milk-

FIG. 1. INFLUENCE OF INJECTIONS OF ANTERIOR-PITUITARY EXTRACT ON MILK-YIELDS OF COWS IN DECLINING LACTATION



From Folley & Young (1945)

The influence of doses of 2.5 g.-equiv. of different types of anterior-pituitary extract, injected at 2-day intervals for 3 weeks, on the milk-yields of groups of cows in declining lactation. The data given are the mean yields for each group over 3-day periods. Group *A*, two cows receiving a crude extract of fresh anterior-lobe tissue. Group *B*, four cows receiving a crude extract of acetone-desiccated anterior-lobe tissue. Group *C*, three cows receiving a crude extract of anterior-lobe tissue which had been desiccated in commercial methylated spirit. On day 29 the dose was doubled (group *C* only). The first injections were given, in each case, on day 15, and the last on day 35. The straight lines are those fitted by the method of least squares to the pre-injection control data for each group.

Abscissae : days
Ordinates : mean milk-yield, pounds/cow/day
I : injections began
II : dose doubled
III : injections stopped

composition encountered was a rise in fat-content in some, though not all, experiments. In this respect prolactin seemed to be more effective than the crude extract (Folley & Young, 1939, 1940; cf. also Sykes, Meulman & Huffman, 1942; Sykes, Gould, Duncan & Huffman, 1944).

With the deterioration of the position of Britain in 1940, it appeared desirable to reopen the question of the hormonal stimulation of milk-production in farm-animals with a view to exploring the possibility of increasing significantly the nation's milk-supply by such means. The results of such experiments with anterior-pituitary extract were not published until 1945 (Folley & Young, 1945; Fawns, Folley & Young, 1945; Folley, Malpress & Young, 1945a). On the results of previous experiments, it was decided to choose a period of three weeks as a convenient period of treatment. Pituitary injections over such a period should induce a substantial increase in milk-yield, and the increase might be expected to be of some persistence. A dose-response curve was then constructed relating the magnitude of a single dose of extract administered to the mean increase in milk-yield over the following two days. From this curve a dose of 10 ml. of extract (corresponding to 2.5 g. of fresh ox anterior-pituitary tissue and containing a total of 150-200 mg. of protein) was found to give a nearly maximal response, and this dose was chosen as suitable for the repeated administration on alternate days over a period of about three weeks. Experiment confirmed the expectation thus derived that the most economic use of the extract was likely to result from the administration of 10 ml. on alternate days over a period of 22 days (Folley & Young, 1945), and accordingly this procedure was followed in all the later experiments.

The results of the further relevant investigations may be summarized as follows:

a. the galactopoietic activity of the crude ox anterior-pituitary extract was not lost if the extract was allowed to remain at room-temperature for 24 hours

b. repeated injections of an extract prepared from whole ox-pituitary gland (including the posterior lobe) had no deleterious effect on pregnant cows and resulted in the usual increase in milk-yield (cf. also Folley & Young, 1938)

c. galactopoietic activity was unimpaired if the anterior-lobe tissue was desiccated in acetone before preparation of the extract

d. desiccation of the gland in ethanol provided material which was almost completely lacking in galactopoietic activity

e. when groups of cows were treated, at 2-day intervals for a period of 2½ weeks, with crude sheep or pig anterior-pituitary extract, a substantial and sustained *depression* of milk production occurred

f. cows at the peak of lactation did not respond to treatment with crude ox anterior-lobe extract which was effective in animals in declining lactation.

The depression of milk-yield in cows resulting from treatment with pig- and sheep-pituitary extracts was provisionally ascribed to rapid antihormone formation to the heterologous glandular material but, since the prestige of the investigators with the farmers concerned had fallen *pari passu* with the milk-yield, it was impossible to obtain the necessary blood-samples from the cows in order to support this provisional assumption. Nevertheless, since antihormone formation had previously been described to ox- or sheep-prolactin in the rabbit (Kabac, 1938; Young, 1938; Bischoff & Lyons, 1939) and to crude ox anterior-pituitary extract in the dog (Dohan & Lukens, 1939; Ennor & Singer, 1942), the assumption appeared to be a reasonable one.

It was disappointing to find that the galactopoietic effect of our ox-pituitary extract could not be demonstrated in animals at the peak of lactation since, if the peak could be raised and such a rise was followed by a decline at a normal rate (or even if the beginning of the decline could merely be delayed), a lasting effect on the milk-production during the whole of the period of decline might be expected. Such an effect would result in a substantial increase in total milk-yield. The results of Asdell *et al.* (1936) are in general agreement with ours, in that these authors found that treatment of lactating goats with prolactin had no obvious effect on milk-secretion if the treatment was begun just after the peak of lactation but, in experiments in which similar treatment was begun later in the lactation period, the milk-yield was significantly raised. As the result of experiments with 510 cows in various stages of lactation, ranging from 1-21 months after calving, Asimov & Krouze (1937) conclude that "the injection of the lactogenic substances is more effective during the first half of lactation (2-6 months)". This, by virtue of omission, may imply that

treatment was less effective during the first month after calving but, in the absence of data regarding the time of occurrence of the peak of lactation in these animals, it is difficult to determine whether or not Asimov & Krouze found any galactopoietic effect when their crude pituitary extract was administered at the peak of lactation. Our own negative results may be explained on the assumption that, during the normal period of steady milk-production after calving (which lasted about 7 weeks in the animals we had under investigations), the factor limiting the output of milk is not the rate of liberation of endogenous anterior-pituitary secretion, though this endocrine factor may become a limiting one in animals which have reached the normal period of decline.

2. Action of Anterior-pituitary Extract in Virgin Animals Brought into Milk by Oestrogen Treatment

De Fremery (1936) reported that virgin goats could be brought into milk by oestrogen treatment followed by injections of prolactin. Later Folley, Scott Watson & Bottomley (1940), Lewis & Turner (1940) and Walker & Stanley (1940) all independently reported that treatment with the synthetic oestrogen diethylstilboestrol alone could bring virgin goats or heifers into milk. Folley & Young (1941a) and Lewis & Turner (1942) reported that combined treatment with the synthetic oestrogen together with anterior-pituitary extract produced more milk than with oestrogen alone. Folley, Malpress & Young (1945b) found that combined treatment with oestrogen and crude anterior-pituitary extract sometimes brought into milk animals which had failed to lactate as the result of treatment with oestrogen alone. Furthermore, the anterior-pituitary extract exerted a significant galactopoietic effect at the peak of oestrogen-induced lactation, and thus was capable of significantly increasing the total amount of milk provided by these virgin animals. However, the practical value of this combined treatment on a large scale was clearly doubtful.

3. Economics of Anterior-pituitary Galactopoiesis in Cows in Declining Lactation

The general conclusion to be drawn from our experiments was (Folley & Young, 1945) that when cows in declining lactation were given treatment by minimally-effective dosage (*v. supra*) of crude ox anterior-pituitary extract (10 ml. subcutaneously on alternate days over a period of 22 days), animals initially producing an average of 18 pounds[1] of milk/day yielded, during the three-week period of injections, 21 % more than would be expected in the absence of treatment; during the two-week period following the cessation of injection on alternate days they gave 15 % above that expected. In round figures, for the total period of five weeks, each cow gave, on the average, 60 gallons[2] of milk instead of an expected 50 gallons. The cost of the experimentally-produced pituitary extract used during the three-week injection-period was 11 shillings per cow. The extra milk obtained, if due allowance be made for the extra food consumed by the treated cows, could be regarded as bringing a profit to the farmer of 1½ shillings per gallon, the total gross profit thus being 15 shillings. The net profit was therefore 4 shillings. The cost of the pituitary glands, and so of the treatment, would undoubtedly be substantially reduced if the process were carried out on a large scale and, even under the expensive conditions of our experiments, would be highly profitable to the individual farmer.

For the process to be applied on a nation-wide scale, consideration must be given to the total supplies of anterior-pituitary tissue continuously available in the country, and to the fractional increase in the nation's milk supply which could be induced, under favourable circumstances, by the treatment. It seems improbable that more than 20,000 g. of ox anterior-pituitary tissue could be collected each week in Britain, which would allow of the treatment of about 2,200 cows for a three-week period. Thus about 38,000 cows could be treated each year, with an extra milk yield of about 380,000 gallons. This is certainly less than 0.05 % of the total fresh-milk supply of the country, and even if treatment with all the available pituitary extract were given during the winter months only, it is clear that no substantial increase in the nation's milk supply would accrue from the employment of pituitary stimulation as a routine process. The situation could obviously not be seriously altered even if large supplies of anterior-lobe tissue were imported from abroad. It should be pointed out, however, that this conclusion did not and does not detract from the fact that, to the individual farmer, the successful use of the process might be of considerable financial advantage.

Since the employment of anterior-pituitary extracts offered no possibility of providing a significant increase in the supply of milk for the country as a whole, two other main lines of research seemed to offer possibly valuable results: (*a*) the development of artificial substitutes for the galactopoietic anterior-pituitary extracts; (*b*) investigation of the large-scale effectiveness of other endocrine extracts, such as thyroid preparations, which were already known to possess galactopoietic activity. These two lines of research overlapped to some extent. The first required further investigation of the nature of the galactopoietic factor or factors in the crude ox anterior-pituitary extract. The earlier researches on this aspect of the subject will first be reviewed.

4. Nature of the Galactopoietic Factors of the Anterior-pituitary Gland

It was early shown by Riddle and his colleagues (Riddle, Bates & Dykshorn, 1933) that anterior-pituitary extracts which were capable of initiating lactation in experimental animals also possessed ability to cause enlargement of the pigeon crop-gland, and it became widely accepted that lactogenesis and ability to induce crop-gland hypertrophy were different activities of one and the same anterior pituitary hormone — prolactin. Nevertheless it was demonstrated that prolactin does not initiate milk-secretion in hypophysectomized guinea-pigs (Nelson & Gaunt, 1936; Gomez & Turner, 1936) although lactation can be induced if anterior-pituitary adrenocorticotropin is administered simultaneously with prolactin (Gomez & Turner, 1937; Nelson & Gaunt, 1937). As Folley & Young (1941b) pointed out, since either prolactin or adrenocorticotropin may initiate lactation in hypophysectomized guinea-pigs

[1] [1 pound = 0.454 kg.—Ed.]
[2] [1 gallon = 4.55 l.—Ed.]

already under the influence of the other hormone, both have an equal claim to the description " lactogenic " under such conditions.

The early experiments of Folley & Young (1938, 1939) revealed little correlation between the galactopoietic activity of anterior-pituitary extracts and their prolactin content. In some instances, extracts which contained no detectable prolactin exhibited a good galactopoietic action in cows in declining lactation (Folley & Young, 1938), while in other experiments crude extracts of acetone-dried sheep anterior-lobe tissue, or of ox ethanol-desiccated pituitary tissue, possessed no galactopoietic activity detectable in our experiments, though such extracts were rich in prolactin (Folley & Young, 1945 ; Folley *et al.* 1945a). Under similar conditions a partially-purified prolactin preparation (5 international units/mg.), injected into cows in declining lactation in a dose which, measured by its stimulating effect on the crop-gland of the pigeon, was seven times as active as crude ox anterior-pituitary extract, possessed only one-third of the galactopoietic activity of the crude extract (Folley & Young, 1940). In general, the galactopoietic activity of our extracts was parallel to their influence on carbohydrate metabolism rather than to their prolactin content. Nevertheless, the possible importance of prolactin in such experiments cannot be eliminated, since the treated cows had intact pituitary glands which might have secreted extra prolactin during the experimental treatment of the animal with anterior-pituitary extracts. In an attempt to stimulate the galactopoietic action of crude anterior-pituitary extract by the simultaneous injection of a mixture of separated anterior-pituitary hormones, in 1940 Folley & Young (unpublished observations), in preliminary experiments involving a single injection of various preparations, found that little or no galactopoietic activity was exhibited in cows given a mixture of small doses of adrenocorticotropin and prolactin. Further investigations by Dr. A. Roy (Roy, to be published) have shown that the injection on alternate days of large doses of adrenocorticotropin containing no detectable prolactin can induce an increment of nearly 20 % in the milk-yield of cows in declining lactation. The administration of commercial prolactin (" physolactin "—Glaxo Laboratories Ltd.) containing 10 international units/mg. induced an increase of only 12 %, while simultaneous administration of the prolactin and adrenocorticotropin produced a 25 % increase. There was, therefore, no evidence of a synergistic action between prolactin and adrenocorticotropin, such as would have been necessary to account for the galactopoietic action of a crude anterior-pituitary extract in terms of its relatively exiguous prolactin and adrenocorticotropin activities.

In view of the importance of adrenocorticotropin in galactopoiesis, attempts were made to find synthetic substances which might possess activity in inducing carbohydrate-storage in fasting animals, similar to that shown by adrenal-cortical steroids possessing an oxygen atom at position 11 of the steroid nucleus. Such activity is exhibited by diethylstilboestrol (Janes & Nelson, 1940) and other oestrogens (Griffiths, Marks & Young, 1941), and many such oestrogens also possess the capacity to increase the insulin content of the rat pancreas (Griffiths & Young, 1940 ; Marks & Young, 1940). Initially, encouraging results were obtained by Marks & Young in 1941 (unpublished observations) with non-oestrogenic derivatives of 4 : 4-dihydroxy-diphenyl ether, and Dr. James Walker kindly synthesized a number of derivatives which might be expected to exhibit such activity (see Walker, 1942). However, the biological assays, involving a determination of liver- and muscle-glycogen contents in treated fasting mice, did not show any consistent activity which might have been of practical significance, and this line of approach was therefore abandoned. It should be mentioned that the extraction of prolactin from sources much more plentifully accessible than anterior-pituitary tissue has been described (Rabald & Voss, 1939), and had it proved possible to prepare non-oestrogenic synthetic substances with carbohydrate-metabolism-stimulating activity, it might have been feasible to combine these with extra-pituitary prolactin preparations to provide large supplies of non-pituitary material possessing, it was to be hoped, some galactopoietic activity.

5. Activity of Thyroid-active Substances : Iodoproteins

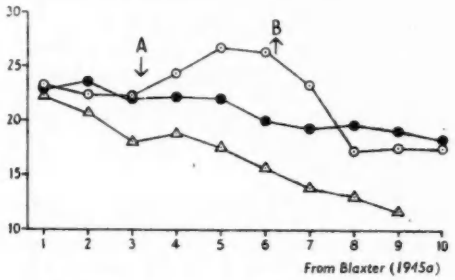
Since, for many years, thyroid preparations had been known to exert a galactopoietic action in cows in declining lactation (Graham, 1934 ; Jack & Bechdel, 1935 ; Jones, 1935 ; Folley & White, 1936 ; Herman, Graham & Turner, 1938 ; Smith & Dastur, 1940 ; Ralston, Cowsert, Ragsdale, Herman & Turner, 1940 ; Hurst, Reece & Bartlett, 1940), our failure to evolve a large-scale method of increasing milk-supplies by the use of pituitary hormones diverted attention to thyroid preparations. In 1939 Ludwig & von Mutzenbecher showed that casein which had been iodinated under certain conditions exhibited thyroid-hormone activity, and that thyroxine could be isolated from the products of hydrolysis of such an iodoprotein. Early in 1940, the present writer suggested (see Barcroft, 1945) that investigations should be made concerning the possible large-scale usefulness of such iodoproteins in the production of milk and, as a result of the subsequent interest of the Agricultural Research Council, large-scale investigations along these lines were planned, but carried out by others. The results of the british investigations were not published until some years later (Blaxter, 1943 ; 1945a ; 1945b), and in the meantime the results of researches in the USA along similar lines had appeared (Turner, 1940 ; Reineke & Turner, 1942 ; Reineke, 1942, 1943 ; Reece, 1944 ; Van Landingham, Henderson & Weakley, 1944 ; Archibald, 1945).

In 1942, Reineke, Williamson & Turner (see Reineke *et al.* 1942) introduced an important improvement in the method of preparation of thyroid-active iodoproteins by demonstrating that the activity of the iodinated material was greatly enhanced by incubation at relatively high temperature (60-70°C.). This procedure was later adopted by the british workers (Pitt Rivers & Randall, 1945).

As the result of extensive investigations, Blaxter (1945a, 1945b) concluded that when active iodoproteins were fed to cows in declining lactation, the increase in milk-yield was least at the beginning and at the end of a lactation-period. In mid-lactation, the percentage response increased as lactation declined ; nevertheless the response in pounds of milk/day fell with a diminution in the initial yield. In early experiments with iodinated " ardein " (ardein is the mixed protein from the ground-nut *Arachis hypogaea* prepared by I.C.I. (Explosives) Ltd., Ardeer, Scotland), material containing 0.88 % acid-insoluble (thyroxine ?) iodine fed in daily doses of 50 g. for three weeks induced an increase in milk-yield 24 % above that expected in the absence of

treatment, and an increase of about 10 % in the percentage fat-content of the milk. Within two weeks of cessation of the treatment, the milk-yield had fallen to a level close to that expected had treatment not been given (fig. 2).

FIG. 2. EFFECT ON MILK-YIELD OF FEEDING IODINATED ARDEIN N4MB TO COWS FOR A PERIOD OF 3 WEEKS



From Blaxter (1945a)

Abscissae : weeks

Ordinates : mean daily milk-yield in pounds

controls

50 g. dose

10 g. dose

A : treatment commenced

B : treatment stopped

With a seven-week period of treatment the response declined after about three weeks of administration of the iodinated protein (Blaxter, 1945a). Later experiments (Blaxter, 1945b) with iodinated casein containing 1.2-2.7 % acid-insoluble iodine, fed in a daily dose of 30 g. over a period of three weeks, again showed a mean rise over the experimental period of about 25 %. With 30 g./day of iodinated casein, the symptoms of hypermetabolism were very pronounced ; with a daily dose of 20 g., the galactopoietic response was only about two-thirds of that with the larger dose, but since only slight symptoms of hypermetabolism were then found, this seemed to be the dose for choice. There was no immediate evidence that the symptoms of hypermetabolism encountered had any lasting deleterious effect on the treated animals.

The american workers have on the whole used smaller amounts of iodoprotein than british investigators. Thus, Reineke & Turner (1942) gave 50-100 g./day of iodinated milk-protein to cows in declining lactation for only three days. while Reece (1944) fed 10 g./day for three weeks, and Archibald (1945) gave 15 g./day for six weeks. The mean increases in milk-yield were of the order of 10 %. In general, the results of the british and american workers are in agreement.

Although increases in the fat-content of milk have frequently been found to follow the administration of thyroid-active substances to cows, the results with iodoproteins both in Britain and in the USA have not been consistent from time to time, though in a proportion of instances significant rises in fat-content have accompanied the increases in milk-yield (Blaxter, 1943 ; 1945b ; Reece, 1944). Archibald (1945) found a significant fall in the casein-content of milk to follow administration of iodoproteins to cows ; on the whole, it may be concluded that the extra milk obtained as the result of treatment with iodoprotein is generally of at least unimpaired quality.

The results at present available concerning the use of iodoproteins as a practical galactopoietic measure suggest that if, as the result of long-term observation of treated cows, no serious disability is encountered, such as diminished fertility or reduced resistance to infection, the measure may become of the greatest importance in dairy husbandry. It must be emphasized that, so far, long-term observations which will conclusively allow the ultimate innocuousness of the treatment to be accepted are not available. With regard to the short-time results, the advantages of the treatment are manifest. Iodoproteins of substantial thyroid activity can be prepared very cheaply on a commercial scale in almost unlimited supply ; the cost of the treatment is very small indeed and it can be applied to large numbers of animals without difficulty. Furthermore, unlike pituitary extracts, which must be administered parenterally, iodoproteins can be given by mouth in the normal food. This fact is of significant practical importance particularly in large-scale work. Developments in the large-scale use of iodoproteins in dairy-farming will be awaited with interest.

It was of some theoretical, and perhaps of practical interest, to know whether the galactopoietic effect of thyroid-active substances and that of crude anterior-pituitary extract would be additive or would be synergistic. With this end in view, Dr. A. Roy has recently determined the effect of giving thyroxine by injection simultaneously with crude ox anterior-pituitary extract to cows in declining lactation. During a three-week period of treatment, the extra milk provided by treatment with the anterior-pituitary extract alone was 19 % ; with thyroxine alone (10 mg. on alternate days), the increase was 16 % ; while with the two treatments given simultaneously the rise was 36 % (Roy, to be published). There was therefore no evidence of a significant synergistic action of the two treatments.

6. Relationship of Galactopoiesis and Other Endocrine Phenomena

Growth, including foetal growth, and milk-production, are processes requiring a special type of metabolic control, in that they both necessitate the preservation from oxidation of foodstuff that would otherwise, in an animal in equilibrium, be oxidized. All our highly active pituitary galactopoietic preparations have also been capable of inducing growth when administered to intact rats and, it may be pointed out, thyroid preparations can induce growth not only in thyroidectomized animals but also, under some conditions, in intact animals. Folley & Young (1938) early pointed out that galactopoietic pituitary preparations possessed anti-insulin activity, and Young (1940, 1945) has emphasized the growth-stimulating activity of his diabetogenic pituitary extracts.

Since growth, galactopoiesis and diabetogenesis all involve a restraint on oxidative processes, it would not be surprising if there were some relationship between the hormonal mechanisms concerned with the control of these phenomena.

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EXPERIMENTAL INDUCTION OF LACTATION

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1 Oestrogenic stimulation of lactation
2 Practical applications
3 Explanations of the dual action of oestrogens
4 Role of progesterone
References

That oestrogens should recently have been used, and with considerable success, for the experimental induction of lactation in non-gravid non-parturient animals is at first sight surprising, for the evidence available hitherto had mostly indicated that the action of these hormones was to inhibit, and not to promote, milk-secretion. This evidence accrued from many sources: lactation, for example, had been frequently observed in guinea-pigs following the cessation of oestrogen injections initially given to produce mammary growth (Nelson, 1937; Laqueur, Borchardt, Dingemanse & de Jongh, 1928); while many authors, following Parkes & Bellerby (1927), demonstrated that oestrogen injections could inhibit established lactation in small mammals (de Jongh, 1933a, 1933b; Smith & Smith, 1933; Robson, 1935; Noble, 1939).

Advantage has also been taken of this function by clinicians, who have found oestrogens a valuable aid in suppressing lactation in women when breast-feeding for one reason or another has become undesirable (*e.g.* Ramos & Colombo, 1938; Barnes, 1942; Walsh & Stromme, 1944), and we may also note that it was in such belief that Nelson was led to propound his oestrogen-inhibition theories explaining the absence of lactation during pregnancy and its sudden onset at parturition (Nelson, 1936).

1. Oestrogenic Stimulation of Lactation.

While the import of these experiments could not be doubted, there were certain anomalous results which suggested that a more complex interpretation of oestrogenic action might prove needful. The work of Frazier & Mu (1935), in which lactation was produced in male rabbits injected with oestrogen, is an example, as also the observation (Anselmino & Hoffmann, 1936) that rat-litters suckled by oestrogen-injected ovariectomized does suffered no diminution of their growth-rates when compared with control-litters.

The bulk of the evidence demonstrating the power of oestrogens actively to initiate milk-secretion derives however, and for practical reasons which must be clear enough, from investigations in which either goats or cows have been used as experimental subjects; it may be noted that the inhibitory action of oestrogens upon lactation is well attested for both these species.

De Fremery (1938) and Trautmann & Kirchhof (1939), working with goats, had already observed lactation following the combined use of oestrogen as a mammary-growth stimulant and prolactin as a specific for milk-secretion when, in 1940, Folley and his co-workers reported the first conclusive demonstration of lactation following treatment with oestrogen alone (Folley, Scott Watson & Bottomley, 1940). These authors, who gave their results more fully in a second paper (Folley, Scott Watson & Bottomley, 1941a), rubbed the udders of virgin goats with an ointment containing 1% of diethylstilboestrol or its dipropionate, and in one case obtained a maximum daily yield of 2 litres of milk in response. These results were independently confirmed by Lewis & Turner (1940), using an oestrogen-injection technique.

Studies on cattle were first reported by Walker & Stanley (1941), who obtained lactation-yields comparable with those of normal parturient animals from two heifers given injections of diethylstilboestrol dipropionate, either alone or in conjunction with testosterone propionate. Folley *et al.* (1941b) also reported small yields from oestrogen-inuncted heifers and, as the result of these pioneer efforts, a great deal of work has since been undertaken with the aim of augmenting available milk-supplies by bringing otherwise valueless, barren animals into production by means of an oestrogen-induced artificial lactation.

2. Practical Applications

The greater part of this subsequent work, together with a few other closely-related papers, has been very conveniently published in a single number of the *Journal of Endocrinology*. Papers by Folley & Malpress (1944a, 1944b), Folley, Stewart & Young (1944), Hammond & Day (1944) and Parkes & Glover (1944) reporting the use of oestrogens administered by various techniques—synthetic oestrogens orally or by subcutaneous implantation, or single injections of different esters—show that these authors all reached very similar conclusions with regard to the merits or limitations of the general treatment and the inadvisability of its immediate widespread application on farms.

Briefly, the treatment was condemned as a practical measure in its present forms, primarily because of the lack of uniformity in the results. Whatever effective oestrogen-dosage was given—and it is known that in this respect the experiments as a whole covered a very wide range—the results in individual cases were quite unpredictable, and yields were too often well below an economically-satisfactory limit, or even nil. On the other hand, many animals gave daily full yields of milk, equal to the best that might have been expected of them as the result of normal calving. Thus, 3 gallons [13.6 l.] a day were often exceeded and, what is more, obtained within two months of the start of treatment when, had a successful mating taken place instead at the same time, seven more months of the gestation-period would still have had to run before any milk at all could be obtained. The method might have an important application therefore in helping a farmer to get winter-milk from a dry animal which he has failed to settle in calf by the autumn—an important consideration in the general problems of milk-production.

A further observation which contra-indicated the use of oestrogens in this way was the occurrence of pelvic changes in the treated animals, more pronounced but similar in character to those accompanying normal parturition; these, when aggravated by the behaviouristic attitudes (repeated coital mimicry) associated with the animals' nymphomaniac condition, led in a number of cases to pelvic fractures unless the animals had been isolated from the herd during the course of treatment.

Yields normally rose to a peak value within one to three months when the implantation method was used, and thereafter declined slowly provided that the oestrogenic stimulus was removed. If the treatment was continued at this point, however, yields fell rapidly, and an oestrogen-inhibitory phase was evidently produced. The original papers should be consulted for a full appraisal of the different experimental techniques from the practical point of view; it is important to note, however, that in all cases where the daily milk-yield was greater than 5 pounds [2.3 kg.], the chemical composition of the milk was normal with respect to all its major constituents (Folley & Malpress, 1944c).

Other reports dealing with this problem of artificial lactation are confirmatory in their import, or provide later supplements to the publications already quoted (Reece, 1943; Day & Hammond, 1945; Spriggs, 1945).

3. Explanations of the Dual Action of Oestrogens

The theoretical implications of the treatment are of great interest: in the first place it has become clear that the effective systemic oestrogen-concentration is of paramount importance in conditioning the response, or lack of response, and a tentative theory put forward by Folley (1941) sought to reconcile the apparently contradictory effects of oestrogens upon lactation by postulating a differential action of the hormone upon the lactogenic-hormone secretion of the pituitary. It was suggested that small concentrations of oestrogen might promote, and large concentrations inhibit, pituitary activity in this respect. Support has since been given to such a theory by the work of Mixner, Meites & Turner (1944), which showed that while the daily injection of 0.25 mg. diethylstilboestrol promoted lactation in non-parous goats, amounts of 1 mg. or more were inhibitory to animals already lactating. A slight amplification of this original theory, in which not one, but two threshold-values of systemic oestrogen-concentration are envisaged as defining pituitary lactogenic activity, might perhaps explain most satisfactorily at the present time the observed practical results. These two thresholds, a lower, below which no stimulus is given to lactogenic-hormone secretion and an upper, above which its secretion is inhibited, will determine the limits of an intermediate zone of stimulatory oestrogen-concentrations within which the pituitary may be regarded as actively releasing hormones of the lactogenic complex. Since Folley & Malpress (1944a) found that from implantations, daily absorptions ranging from 4-24 mg. could be associated with copious lactation, while absorptions falling well within this range often had negligible effect, it becomes necessary to postulate either that the stimulatory and inhibitory threshold-concentrations of oestrogen in the blood can vary widely both absolutely and relatively, between individual animals of the same species; or that the endogenous-oestrogen secretion of the animal is, in its turn, subject to great individual variations, or perhaps that rates of synthetic-oestrogen excretion and catabolism may differ and systemic oestrogen concentrations be affected accordingly.

Until further work has been done on the metabolism of the synthetic oestrogens, little can be said on the significance of the last possibility, but of the two other explanations the first is undoubtedly the more attractive, for there seems but little likelihood—having regard to the inactive ovarian states induced by oestrogen treatments—that any appreciable endogenous oestrogen will be present to supplement the hormone exogenously applied. The double-threshold theory, moreover, does suffice to explain many of the observed results quite convincingly: it will be clear, for instance, that, where the threshold-values are very different, there will be a large range of oestrogen-concentrations able to promote lactation, whereas when they are close together the stimulatory range will be small and the difficulty of bringing such an animal into artificial lactation will be enormously increased; that such difficulties should exist tallies with field-experience. Further, the sudden increase in yield, noticed when oestrogen treatment is stopped after a peak yield has been obtained and an inhibitory phase of lactation-decline produced, may well be caused by a transitory passage of the now-falling systemic oestrogen-concentration through the stimulatory range, before reaching the still-lower zone where no effect at all is exerted on the pituitary.

4. Role of Progesterone

Apart from the effect on lactation, however, the importance of the type of glandular tissue which develops after simple oestrogen treatment cannot be overlooked. In the treated animals, lactation must clearly be both preceded and accompanied by mammary growth, and although there are some indications that species may differ one from the other regarding the exact stimuli required for normal development, recent experiments on the rabbit (Lyons & McGinty, 1941; Scharf & Lyons, 1941) have suggested that a definite ratio of progesterone to oestrogen is essential for such development, and that an imperfect balance between these two hormones may lead to a stunted or otherwise abnormal parenchyma.

We might argue from this that in the goat or cow a more abundant lactation might be induced by combining our simple oestrogen treatment with progesterone administration, and experiments have been devised by Mixner & Turner (1943) to test this hypothesis. They found, by the examination of histological and of dissected sections, that the lobule-alveolar response in the goat to treatment with diethylstilboestrol alone was in fact rarely typical of the development in the normal gland, and that in those cases in which progesterone was also given, the approach to a normal histological structure was much closer. Their results imply, therefore, that although oestrogens given alone may be suitable for the induction of lactation in non-breeding dairy animals, the chances of success should be enhanced by the simultaneous administration of progesterone. The validity of interpretations based on comparative studies of histological sections of lactating mammary tissue must, however, depend on the trustworthiness of the techniques employed. In particular, it is to be doubted whether small specimen blocks

cut from the udder can be considered in any way representative of the whole gland ; sectioning the whole udder, on the other hand, involves special problems of fixation demanding suitably adapted procedures. Recognizing this, Cowie, Folley, Malpress and Richardson, in recent and unpublished work, have started to re-investigate this question of the role played by progesterone in the development of the mammary gland of the goat, milking the animals as completely as possible before mammectomy, and afterwards fixing the whole gland by immediate arterial perfusion. By this means it becomes possible to examine histologically transverse sections of the whole udder, and although a sufficient number of animals has not yet been treated, the authors are at present inclined to the view that there is no significant quantitative superiority of the alveolar tissue of animals treated with both progesterone and oestrogen, over that taken from animals injected with oestrogen alone. It remains, of course, a distinct possibility that the ratio of the two hormones used in these experiments may not be optimal for mammary growth in this species or, again, that the quantitatively uncertain, and unassessed, effect introduced by the secretion of substances having progestational activity by the adrenal gland, may be influencing the results—as indeed it may be doing to a variable, but significant degree, in all experiments of this kind.

* * *

As an addendum it is interesting to note here the limited success encountered by various authors in their attempts to develop and initiate lactation in the male gland by oestrogen treatment (Hogreve, 1936 ; de Fremery, 1938 ; Folley, Scott Watson & Bottomley, 1941a). Folley & Malpress (unpublished work), in an attempt to improve upon these failures, implanted tablets of both progesterone and oestrogen in a steer. There was only a slight development of the gland, and milk-secretion was limited to a few millilitres daily for a period of a few weeks.

* * *

The question of the galactopoietic activity of pituitary extracts is considered elsewhere[1] in this publication but it is of importance here to recall the interesting experiments of Folley & Young (1941), Lewis & Turner (1942), and Folley, Malpress & Young (1945), in which goats or cattle receiving apparently-inhibitory doses of oestrogen were induced to lactate by the additional use of pituitary preparations containing prolactin and probably other components also of the lactogenic-hormone complex. These experiments emphasize the connexion between inhibitory oestrogen-titres and the suppression of the pituitary principles which initiate and maintain lactation, and indicate that we might certainly hope for a far greater success in our field-trials were pituitary extracts available in greater quantity.

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Undoubtedly, then, our further advance in solving the problems of the artificial induction of lactation depends on a better understanding of the quantitative interdependence of oestrogen and progesterone in mammary growth, and of oestrogen and the pituitary lactogenic hormones in the control of lactation. This knowledge will need to be general, and yet also to allow particular reference to the individual animal, and it would seem unwise, until such additional information becomes available, to prophesy any outstanding advances in our efforts to make the artificial induction of lactation in barren animals a factor of real importance in commercial milk-production.

[1] [*BMB* 1104]

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CLINICAL TREATMENT OF HYPOGALACTIA BY HORMONAL METHODS

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A Varieties of hypogalactia
B Controls treated by non-hormonal methods
C Hormonal methods
1 Dried thyroid gland
2 Anterior-pituitary extracts
3 Oestrogens
D Conclusions
References

Since the discovery of ductless glands and of hormones, various attempts have been made to use them to influence the course of lactation in women. Owing to the confused state of our present knowledge concerning the effect of hormones on lactation in women, Prof. F. G. Young suggested that the matter should be investigated. With the support of the Medical Research Council, and on the clinical advice of Mr. J. M. Wyatt, F.R.C.S., F.R.C.O.G., and later of Mr. A. J. Wrigley, F.R.C.S., F.R.C.O.G., such an investigation was begun at St. Thomas's Hospital in 1944, and extended in 1946 to University College Hospital by the kind permission of Prof. F. J. Browne, and subsequently of Prof. W. C. Nixon. The following is a review of the results obtained.

A. VARIETIES OF HYPOGALACTIA

There are two classes of dairy-cows—the "sprinters" and the "stayers". In the early weeks of lactation, the sprinters are the prize milkers, but their milk-yield ceases very early. The stayers are the good dairy-cows, who give a steady moderate yield of milk over a longer period. The same is true in women. Women can be divided into five classes of milkers:

1. *Stayers.* As in cows, there are women who give, over a period of about 9 months, a daily output of milk which is just adequate for the needs of the infant. This is normal lactation, and needs no treatment.

2. *Sprinters.* As in cows, these women yield very large quantities of milk during the first 2-4 weeks of lactation, and then quite suddenly the supply ceases at about the 6th week of lactation.

3. *Stickers.* These women produce sufficient milk to satisfy their infants during the first 2-3 weeks of life. If the infants are test-fed daily during the first 2 weeks, and then once a month up to the 6th, it is found that the milk output in these women rises to a certain level, and then remains more or less at that level throughout the six months of lactation. The infants need to be partly bottle-fed from about 4 weeks of age. Test-feeding during the puerperium shows that the milk in these women does not reach 10 ounces[1] on the 5th day, nor 16 ounces on the 10th day; whereas, in the sprinters and stayers, the total milk-yield on the 5th day is over 10, and on the 10th day is over 16 ounces.

4. *Non-starters.* These patients produce little or no milk on the 5th day of the puerperium. If the breasts are soft and flabby, a little colostrum can be expressed. If the breasts are lumpy and painful, only a few drops of fatty secretion can be expressed.

5. *Abscess-producers.* These patients usually belong to the sprinter-class. In the puerperium, mastitis often causes their lactation to fail. In the later months of lactation (especially during the first three months), breast-abscesses cause their lactation to fail.

Hypogalactia occurs in the puerperium among the patients who are either stickers or non-starters. It is diagnosed by a total output of less than 10 ounces on the 5th day, or less than 16 ounces on the 10th day of the puerperium.

B. CONTROLS TREATED BY NON-HORMONAL METHODS

82 puerperal women were used as controls. They were divided into five groups. One group had no treatment. The others were treated at random with either massage, a proprietary galactagogue, inactive pills or daily intramuscular injections of physiological saline. The massage and inactive pills were given only from the 5th or 6th day of the puerperium until discharge from hospital. The saline injections were given once daily on 5 consecutive days. The proprietary galactagogue was given until lactation had failed, or until the sixth month of lactation was reached.

The mean output for the 82 controls was 5.9 ounces per day before treatment started. It rose to 8.0 ounces per day during treatment. When the infants were one month old, it had risen to 8.4 ounces per day, and then began to fall. When the infants were six months old the mean output per day had fallen to 3.5 ounces.

C. HORMONAL METHODS

1. Dried Thyroid Gland

The earliest known attempt to use hormones to stimulate lactation was made by Hertoghe (1896), who reported an increase in the milk-yield, both in women and in cows, when they were given dried thyroid-gland substance by mouth. His work, however, was not followed up by others, and was forgotten. Recently, interest in dried thyroid gland has been revived by reports of its use as a galactagogue in cows. During the last few years, several clinicians have unsuccessfully treated deficient lactation in women with tablets of dried thyroid gland by mouth. Their results do not seem to have been published. On enquiry, it was found that the dose of dried thyroid gland used was ½-grain[2] tablets twice or three times daily by mouth, and that the infants were more than 2 weeks old when the treatment was begun. At St. Thomas's Hospital it had been found impossible to stimulate failing lactation with dried thyroid gland after the end of the puerperium, whether the patients belong to the classes of milkers called sprinters,

[1] [1 ounce = 28 g.—ED.]
[2] [1 grain = 66 mg.—ED.]

stickers, or non-starters, or have failed because of a breast-abscess.

A series of 14 women, suffering from hypogalactia in the puerperium, was given by mouth ½-grain tablets of dried thyroid gland (thyroideum siccum, B.P. 1932) four times daily, starting on the 6th or 7th day. The mean increase in milk-yield was the same whether the treatment ceased on discharge from hospital, or whether it was continued until lactation had failed, or until the infant was six months old. The mean increase in the milk-yield during treatment was only slightly better than it was among the controls. Instead of decreasing after the 4th week of lactation, as it did among the controls, the mean daily milk-yield continued to rise up to the 6th week of lactation, and then remained steady up to the sixth month.

Following this experiment, 100 puerperal women suffering from hypogalactia were divided into six groups. Each group was given at random varying doses of dried thyroid gland by mouth. The dosage was from 4-9 grains of dried thyroid gland per day. The treatment lasted from 4-8 days, ending when the patient was discharged from hospital, or when the milk-yield had risen to 16 ounces per day. The increase in the mean output per day during treatment was highest (150%) among the patients receiving 8 grains of thyroid per day. The highest percentage (50%) of patients reaching an output of 16 ounces per day occurred among those who were given daily either 6 or 7 grains of dried thyroid gland. Further test-feeding of the infants of those women who had attained an output of 16 ounces before discharge from hospital has shown that the rise in output continues at least up to the third month. This experiment is too recent for any more to be said of it at present.

Twenty-five puerperal women suffering from hypogalactia were given by mouth 1.6 mg. of thyroxine per day for from 3-5 days. The mean increase in milk-output was equivalent to that of the women who had received 8 grains of thyroid per day. Fifty per cent. of these women were producing 16 ounces of milk per day before discharge from hospital, and their output continued to rise after discharge.

Why some patients respond so well to dried thyroid gland and thyroxine, while others show little or no response, is at present unknown. In some patients the pulse-rate rose to 100 per minute, but no signs of thyrotoxicoses were encountered.

2. Anterior-pituitary Extracts

Stricker & Grueter (1929a ; 1929b) discovered that once the mammary glands had developed, injections of an extract of anterior-pituitary gland caused the secretion of milk to begin. A hormone, prolactin, has been isolated, and Kurzrok, Bates, Riddle & Miller (1934), Ross (1938), Kenny & King (1939), and Stewart & Pratt (1939) have all reported a certain amount of success in stimulating lactation by injecting it. The success reported by these observers has not, however, been confirmed by others, and prolactin has fallen into disuse.

At St. Thomas's Hospital, 67 puerperal women suffering from hypogalactia were treated with crude anterior-pituitary extract. The extract was injected intramuscularly once daily on 5 consecutive days. Injections of physiological saline were used as a control. The extract was prepared as described by Young (1941), and was supplied by Glaxo Laboratories Ltd. The results were similar to those in the control cases.

Similar results were obtained with women in the later weeks of lactation.

3. Oestrogens

a. Ante-Natally

1. *Effect on nipples.* Attempts to stimulate the growth of nipples with oestrogens have resulted in complete failure.

The most extreme cases of inverted nipples will, however, become everted after treatment by inunctions of 5% stilboestrol in arachis oil into the base of the nipples 4-6 times daily during the last 4 weeks of pregnancy. Weaker solutions of stilboestrol in arachis oil, and control inunctions of arachis oil alone, do not have the same effect.

2. *Effect on subsequent lactation of antenatal administration of oestrogens by mouth.* A series of patients was given 5 mg. of hexoestrol by mouth every 4 hours for 1-3 weeks before delivery. Where the subsequent labour was normal, the onset of lactation was not delayed, and the secretion of milk was often copious. Where operative interference was necessary, or where the labour was long and difficult, the onset of lactation was often delayed and the secretion scanty, sometimes being even absent.

Among the controls who had not had oestrogens antenatally, it was found that a higher percentage of deficient lactation occurred among women who had had uterine inertia, forceps-delivery, caesarean section or episiotomies. It would seem therefore, that it is not the oestrogens which delay the onset of lactation, but the difficult labour.

b. Post-Natally

1. *Engorgement of the breasts.* The too-rapid onset of lactation at the 2nd or 3rd day of the puerperium causes engorgement of the breasts. It was found that this could be controlled by oestrogens. The breasts usually become engorged during the 2nd or 3rd night of the puerperium. This can be prevented by leaving a 5 mg. tablet of hexoestrol or stilboestrol beside the patient on the 2nd evening, and instructing her to take it with a tumbler of water as soon as she feels a sensation of tightness in her breasts. If the pill has been taken when the next feed is due, further 5 mg. tablets of hexoestrol or stilboestrol should be given after every breast-feed until the Sister or Medical Officer has seen the patient, and has decided that the risk of engorgement is past. Anything from 3 to 18 tablets may be necessary. It is better to err on the side of too many tablets than too few. This treatment does not suppress lactation, but keeps the milk flowing freely, and prevents failure in those women who have the ability to lactate normally. The infant should on no account be removed from the breast during this treatment.

2. *Lumpy breasts.* Lumpy breasts in the puerperium can be cured by 5 mg. tablets of stilboestrol or hexoestrol, or by 1 mg. tablets of dienoestrol. The tablets should be given with a tumbler of water after each breast-feed, *i.e.*, every 3-4 hours, until the lumps have gone. The infant should not be removed from the breast during the treatment. The output of milk increases in those women who have the ability to produce milk. There is no change in output where the ability to produce milk is absent.

3. *Cracked nipples.* Five per cent. stilboestrol in arachis oil, rubbed into the crack, will heal it in a few days. Until

the crack is healed, the patient should wear glass shells, in order to keep the nipple dry, and to keep the clothes from sticking to the crack. The stilboestrol in oil must be washed off before each breast-feed, and re-applied afterwards. As much as possible must be rubbed into the tissues. If the surface of the nipple is left covered with oil, it is liable to give rise to a rash. Stilboestrol has been used by others, but the results do not appear to have been published. The healing-time was found to be much quicker than among the control cases.

4. *Lactorrhoea.* Lactorrhoea is common in the first weeks of lactation. If it is excessive and continues after the 3rd week of lactation, it may give rise to a superficial breast-abscess, or to failure of lactation. It is commonest among the sprinter class of milkers. It can be cured from the 4th week of lactation by giving the mother 5 mg. of hexoestrol or stilboestrol by mouth after every breast-feed over a period of 5-7 days. When cured it never seems to recur. It cannot be controlled during the puerperium, and most cases spontaneously recover in the 3rd week of lactation. If lactorrhoea and failing lactation are present together in the later weeks, treatment with oestrogens increases the milk-yield and seems to prevent subsequent failure. This treatment also prevents superficial breast-abscesses which start as a staphylococcal infection of the Montgomery follicles owing to the continual moistness of the skin of the areola.

5. *Threatened breast-abscesses of the deep glandular type.* This kind of abscess may occur from the 2nd week of lactation onward. The mother usually belongs to the sprinter class of milker. Hexoestrol (5 mg. every 4 hours) was found to cure the condition, provided treatment was commenced before the pressure inside the lobules had destroyed the cells. If the treatment is started within 1-2 days of the appearance of the lump, the condition can be cured in a few days. The temperature drops within 12 hours, and the lump becomes less painful, and finally vanishes. If the condition is more advanced when treatment is begun, it may be necessary to give the patient, every 4 or 3 hours, 5 mg. of hexoestrol for as long as 3 weeks. Hexoestrol does not produce in these women withdrawal-bleedings from the uterus. The infant should not be removed from the breast during treatment. Patients who have been cured show a tendency to recurrences. As many as 7 attacks have been noted in the same woman during the six months of her lactation.

Patients who belong to the sprinter class of milkers should be discouraged from expressing their milk after feeding the infant, as this leads to early failure. Instead, they should be provided with a box of 5 mg. tablets of hexoestrol, and be told to take one pill after each breast-feed, if they feel that their breasts have not been emptied by the infant. In this way breast-abscesses of the deep glandular type can be prevented.

Failure of lactation can be prevented in the sprinter class of milkers by discouraging expression of the breasts after feeds, together with periodic short courses of oestrogens. So long as the infant is kept at the breast, oestrogens do not seem to suppress lactation. It seems to be the pressure inside the lobules that suppresses lactation, and in some way unknown at present the oestrogens can control this pressure, provided the cells of the lobule are living. Barnes[3] (1942) has noted how difficult it sometimes is to suppress lactation with oestrogens where the infant is not suckling. Arbarbanel (1939) doubts whether oestrogens do suppress lactation where the infant is suckling.

One week's course of oestrogens after each breast-feed can also be used to control the force with which the breast sprays the milk into the infant's mouth. Infants belonging to the sprinter class of mother can in this way be prevented from choking at the breast and from getting the "wind".

6. *Infantile mastitis.* Infantile mastitis sometimes becomes so advanced that incision is necessary. This can be prevented by applying 5 % stilboestrol in arachis oil on lint to the infant's breasts, and leaving the lint in position for 24 or 48 hours. Then gentle pressure causes the milk to spray out, and the mastitis disappears and does not recur. The fluid expressed has been proved to be milk.

D. CONCLUSIONS

In conclusion it can be said that there are five classes of milkers among women, and that, at present, there are only two hormones which can be used for the treatment of hypogalactia.

1. *Stayers.* In these women the production of hormones is normal, and they successfully feed their infants without difficulty.

2. *Stickers and non-starters.* These women seem to be deficient in thyroid secretion, and therefore need intensive thyroid therapy in the puerperium in order to cause them to start lactating normally. Treatment after the 12th day of the puerperium has been found to be useless.

3. *Sprinters and abscess-producers.* These women need to be intermittently given oestrogens throughout the whole six months of lactation, in order to prevent breast-abscesses and early failure of lactation.

4. *Deformed and cracked nipples* can be cured by local inunctions of oestrogens.

5. An extract of the anterior-pituitary gland has not been found to increase milk-production in women suffering from hypogalactia.

6. Infantile mastitis can be cured by local application of oestrogens to the infant's breasts.

[3] [See also article (*BMB* 1107) by Barnes in this number.—ED.]

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HORMONAL INHIBITION OF LACTATION

With Special Reference to Man

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One of the striking contributions of endocrinology to clinical obstetrics has been the use of hormones for the inhibition of lactation. Before the discovery of these specific substances the standard method consisted in binding the breasts, restricting fluid-intake and administering saline aperients. In spite of these measures, which have obvious disadvantages for the puerperal woman, the patient would often have to endure painful engorged breasts for several days. The symptoms might be so severe as to necessitate the administration of analgesic drugs.

Endocrine control of lactation has been dealt with elsewhere[1] in this series (Folley, 1947a, 1947b).

Oestrogens

On the basis of experimental findings, it was suggested that oestrogenic hormones might be used for the inhibition of lactation in puerperal women. This suggestion appears to have been first made by Sawizki (1935). Hoffmann (1937) claimed that lactation could be inhibited in women by the use of follicular hormone. Foss & Phillips (1938) obtained satisfactory results in 62 cases with oestradiol benzoate, giving a total dose of 10,000 international units. They found that oestrogens were also useful for flushed and engorged breasts, relieving the symptoms without interfering with lactation. Lehmann (1938) used oestradiol benzoate and found that 100,000 international units given by injection in the first 24 hours post partum inhibited lactation in 91% of cases. Inhibition of established lactation was obtained in 89% of cases with 200,000 units, but in only 50% with 150,000. Jeffcoate (1939) gave oestrone by mouth in doses of 2-6 mg., gradually decreasing the dose over 1-3 days. He found that it was usually necessary to supplement this by 1-2 mg. of oestradiol benzoate by injection. Adrian (1938) used 20,000 international units by injection, repeating the dose up to a total of 60,000 units. Pain and tension in the breasts were relieved, but in 43% of cases there was slight secretion of milk. Ramos & Colombo (1938) also showed that lactation could be successfully inhibited by naturally-occurring oestrogenic hormone.

Since the discovery of the synthetic oestrogens it has been shown that these substances are capable of reproducing the biological and clinical effects of the naturally-occurring oestrogens. They can be produced relatively cheaply and are in most cases as potent, if not more so, when given by mouth as when injected. Thus, they stand in contrast to the naturally-occurring oestrogens, which are generally very much less potent by mouth and are therefore best administered parenterally.

In view of the success achieved with naturally-occurring oestrogens, it was obvious that synthetic oestrogens were likely to prove useful for the inhibition of lactation. Reports of success with stilboestrol appeared from Winterton & MacGregor (1939) and from Wenner & Joël (1939). Mucklé (1940), using stilboestrol, found that though initial success was achieved with 5 mg. given three times daily, the breasts filled in 40 % of his cases in 4-5 days and further treatment was necessary. Mendel, Goldman & Caire (1941) also claimed satisfactory results with stilboestrol.

Stewart & Pratt (1941) suggested that inhibition of breast-engorgement is not synonymous with inhibition of lactation. Stilboestrol, natural oestrogens and testosterone may all be used to prevent engorgement. Lactation may be diminished temporarily with stilboestrol, though individuals vary in this respect. A negligible effect on lactation was noted with 250,000 international units of oestrone and 125 mg. of testosterone.

Abarbanel & Goodfriend (1940) discovered, in a study of 315 lactating women, that doses of up to 1,000 mg. of stilboestrol were well tolerated. They also found that stilboestrol did not inhibit the onset of lactation and, in doses of 500 mg., did not inhibit established lactation provided that the stimulus of suckling was present.

Connally, Dann, Reese & Douglass (1940) studied the effect of stilboestrol in 200 puerperal women, finding no toxic effects even with large doses. They found that the onset of normal lactation was delayed in cases receiving stilboestrol, but that there were no cases of engorged or painful breasts among their patients.

Abarbanel & Klein (1941) gave stilboestrol to three groups each of 50 puerperal women. In the first group, which consisted of normally-lactating women, no effect was noted. In the second group stilboestrol was given 3-10 days post partum, and it was found that the onset of lactation was not affected, provided that the infant was suckling. In the third group, consisting of women who were not suckling, it was found that stilboestrol prevented painful breasts in 87 %.

Thus, by the end of 1941 it was established that substances with oestrogenic properties, whether naturally occurring or synthetic, could be used for the inhibition of lactation and for the prevention and treatment of breast-engorgement. At this time an investigation to test the effects of the new synthetic oestrogen dienoestrol was carried out by the present author (Barnes, 1942). It was decided to try the effect of the new substance for the inhibition of lactation, comparing it with stilboestrol and hexoestrol, in order to test the relative potency of the three substances. Trials were carried out in 134 cases, 81 receiving stilboestrol, 37 dienoestrol and 16 hexoestrol. Ultimate success with regard to lactation was obtained in all cases, though in about a quarter it was necessary to repeat the five-day course of treatment, as the breasts filled up after discontinuing treatment. The dosage was varied in an endeavour to find an optimum. Most of the patients received stilboestrol, a total dosage of 30 mg. usually

[1] [See *BMB* 1100, 1101.—ED.]

being given, starting with 5 mg. twice daily and gradually diminishing the dose down to 1 mg. twice daily. Dienoestrol was used with caution and in much smaller doses than stilboestrol and hexeostrol. This was because dienoestrol was being used clinically for the first time. Experimental work with mice by Emmens (1938) had suggested that dienoestrol was at least ten times as potent as stilboestrol when given by mouth. Also it was not certain that dienoestrol was free from harmful effects.

It must be emphasized that even in cases where complete success was not achieved, that is in 60 out of the 134 patients, the symptoms complained of amounted to no more than a slight fullness of the breasts or temporary leakage of milk. Results were better when treatment was begun within one day of delivery than when it was started later. They were also better in patients in whom pregnancy had advanced beyond the 32nd week than in those where termination had occurred in the earlier months. No toxic effects were noted, apart from transient nausea in 3 patients.

It was impossible to give more than a vague idea regarding the relative potency of the three substances, since the series was too small and thus opportunities for varying dosage were too limited. It was suggested that stilboestrol was more potent than hexoestrol, and that dienoestrol was more potent than either. The latter result has not been confirmed by subsequent work by others, using dienoestrol for other purposes, and it is now suggested that dienoestrol is three times less potent than stilboestrol. Nevertheless, the value of these three synthetic oestrogens for the inhibition of lactation is now established.

Triphenylchloroethylene, another synthetic oestrogen, was also used in my series in a few cases. Macpherson & Robertson (1939) first demonstrated the oestrogenic properties of this substance and showed that it could be used for the inhibition of lactation. Moir (1942) reported a series of nearly 50 cases where triphenylchloroethylene was used for the inhibition of lactation. The dose used was one tablet of 500 mg. twice daily for 4 days, followed by one tablet daily for 3 days. A test of 250 mg. in a single injection in oil was not successful, but in the cases where the substance was given by mouth there were no failures. Moir concluded that the question of the ideal oestrogen for the inhibition of lactation may be largely one of the relative cost of the different products.

Kurzrok, Birnberg & Livingston (1942) gave ethinyl oestradiol by mouth to 59 puerperal women for 3-4 days. Doses of less than 1.5 mg. daily gave only moderate results, but with 1.5 to 2.4 mg. daily for 3-4 days, results were excellent.

Diddle, Nagyfy & Sells (1942) compared the effect on breast-engorgement of α-oestradiol in propylene glycol with that of stilboestrol. Comparable total dosage of the two drugs gave similar results, but α-oestradiol had to be given more frequently and was more expensive than stilboestrol.

Murphy (1943) used octofollin in 25 women for inhibition of lactation, giving 5 mg. three times daily for the first 4 postpartum days. Results were excellent and no toxic effects were observed.

Four further papers giving the results of the use of stilboestrol for the inhibition of lactation appeared in 1944 and 1945. Walsh & Stromme (1944) obtained excellent results in 190 cases, with controls, finding that 20 mg. of stilboestrol given in a diminishing dosage for three days gave striking relief of pain and engorgement as compared with controls. The effect was slight once lactation was established. Meek & Murby (1944) compared the effects of stilboestrol and natural oestrogen on two series each of 30 cases. Both were found to be efficient and well tolerated, but the effect was slight once lactation was established. Brown & Grant (1944) gave stilboestrol and tablets containing a placebo to alternate women who were normally suckling. The authors found that stilboestrol was well tolerated and did decrease breast-engorgement, but at the expense of lactation. Fields (1945) found that stilboestrol was effective in aiding cessation of lactation, but depressed milk-secretion, in spite of suckling, when given to normally-lactating women.

Prescott & Basden (1944) found that a single intramuscular injection of 12.5 mg. of hexoestrol dipropionate, given in the first 3 postpartum days, was effective in inhibiting lactation in 66 % of a series of 44 mothers. Further treatment was needed in only 34 %, and secondary filling occurred in only 7 %. The authors claim that their results compare favourably with those of other workers who gave oestrogens by mouth, and state that in their experience oral treatment was less successful than treatment by injection.

To sum up, it may be said that any substance which has oestrogenic properties may be used for inhibiting lactation. The question of the choice of oestrogen may eventually prove to be largely one of cost. Synthetic oestrogens have the advantage of cheapness and are also easily given by mouth.

Testosterone

It has been shown experimentally that testosterone inhibits lactation, and clinical trials have shown that this substance may also be used for inhibition of lactation in puerperal women.

Kurzrok & O'Connell (1938), Birnberg, Kurzrok & Klor (1940) and Siegler & Silverstein (1940) all used testosterone propionate for this purpose. All obtained good results, and Siegler & Silverstein considered that testosterone is better for the inhibition of lactation than stilboestrol, claiming that stilboestrol causes afterpains and excessive lochia. This does not appear to be the experience of other workers who have used stilboestrol, and the results with testosterone do not appear to be as good as those with stilboestrol. Better results were obtained by Abarbanel (1939), who gave testosterone propionate in doses of 10 mg.-5 mg. intra-muscularly and, one hour later, 5 mg. subcutaneously. He found complete relief of breast-pain in 92 % of 50 patients, but found that, provided suckling was continued, there was no effect on lactation.

Kushner (1942) gave 25 patients methyl testosterone by mouth in doses of 30 mg. three times daily for 3 days, a total dosage of 270 mg. Success in the form of complete inhibition of lactation was obtained in 23 cases. Kushner recommends methyl testosterone by mouth as a substitute for testosterone propionate administered by injection, or percutaneously, for postpartum inhibition of lactation.

Lass (1942) also used methyl testosterone orally, giving 250-300 mg. in divided doses over a period of 36 hours, beginning 36 hours after delivery. He found that the course of the puerperium was unaffected and that patients were more comfortable than when older methods were used.

Duckman & Turino (1942) used testosterone, giving 150 mg. in 5 doses of 30 mg., beginning on the 4th postpartum day. Good results were obtained in 88 % of cases.

Diddle (1941) compared the use of stilboestrol and testosterone propionate for the inhibition of lactation. Good results were obtained with both substances, though two

patients who were receiving stilboestrol exhibited toxic effects. The dosage of testosterone propionate, 25 mg. on 3 alternate days, or a total of 75 mg., was smaller than that used by other workers.

Jeppson, Kasabach & Kanter (1942) studied the effects of testosterone propionate on lactation and found it of little value in preventing breast-engorgement. It was found to delay and depress lactation. For inhibition of lactation they found little to choose between testosterone propionate and stilboestrol.

It may be concluded that though testosterone may be successfully used for the inhibition of lactation, it has no special advantage over the oestrogens and is much more expensive. Testosterone propionate has the additional disadvantage of requiring parenteral administration.

Discussion

That the administration of appropriate hormones, or their synthetic analogues, does inhibit lactation, or at least prevent painful engorgement of the breasts in non-lactating, puerperal women, is an undoubted clinical fact. The mechanism of this remains obscure, the more so because it is known that oestrogenic hormone may exert both mammogenic and lactopoetic effects, at least in certain animals. Abarbanel (1941) suggested that painful engorgement of the breasts and lactation are not synonymous, though they may occur simultaneously.

Certain experimental observations may be quoted, though they throw little light on the general problem. Hamilton (1937) claimed that testosterone causes inhibition of the hypophysis, with histological degeneration. Reece & Mixner (1939) showed that administration of testosterone increased the lactogenic-hormone content of the anterior pituitary. They injected testosterone daily for 15 days into sexually-mature, spayed female rats. The lactogen content of the pituitary increased by 40 %, and there was extensive development of the lobular-alveolar system, this effect occurring apparently through the anterior pituitary. Mixner & Turner (1942) showed that progesterone, desoxycorticosterone-acetate, dehydroandrosterone, stilboestrol, acetoxypregneninolone and methyl testosterone all stimulate growth of the mammary-alveolar system, while testosterone and testosterone propionate do not. Meites & Turner (1942a) suggested that the decrease in lactation due to natural oestrogens, stilboestrol and testosterone propionate was due to decrease in the secretion of anterior-pituitary hormones other than lactogenic hormone. It was suggested that these hormones were in some way essential for milk-secretion. The same authors (Meites & Turner, 1942b) showed that progesterone had no effect in the guinea-pig on the lactogen content of the pituitary, but that oestrogenic hormones increased pituitary lactogen. Meites & Turner (1942c) suggest that progesterone falls first, just before parturition, and gives ascendancy to oestrogen, which stimulates the production of lactogenic hormone. This does not seem a very convincing explanation of what is undoubtedly a complex mechanism, and further work seems necessary to clarify the position.

The clinical facts are, however, proved without question and only two further points require discussion. First, are hormones given in the puerperium in any way harmful and, secondly, which is the best preparation for clinical use?

The effect of hormones on puerperal women was studied by Rutherford (1942). He studied three groups, each of 12 patients. One group was taken as a control. The second received 10 mg. stilboestrol daily for 12 days. The third group received 10 mg. methyl testosterone orally for the first 12 days. He claimed that involution was delayed by stilboestrol and not by methyl testosterone. Endometrial biopsy showed that repair of the endometrium was hastened by stilboestrol, but delayed by methyl testosterone. Regeneration of the epithelium, but not of the stroma, was hastened by stilboestrol but delayed by methyl testosterone. The myometrium was unaffected. The effect of stilboestrol was lost within one week, and that of testosterone within three weeks after withdrawal. Thus, apart from the delay in involution, always an extremely difficult matter to assess accurately and therefore open to question, there was no evidence of any harmful effect.

Connally (1943) studied the effect of stilboestrol on puerperal women. He claimed that it tended to reduce the incidence of postpartum pyrexia, possibly due to the increased vascularity of the uterus, or to an effect on the myometrium, or to rapid regeneration or to alteration in vaginal pH. He found that suppression of lactation tends to occur and concludes that this precludes the routine employment of stilboestrol in the puerperium. Pregnant and puerperal women tolerate large doses of stilboestrol, such as would cause toxic symptoms in the non-pregnant. Bromberg (1942) emphasized this fact. He found no effect from 275-445 mg. of stilboestrol, while other workers have given as much as 1,000 mg. without any signs of toxicity. Bromberg concludes that pregnant women must detoxicate stilboestrol in some way, since one of his patients who showed no toxic reactions when pregnant, reacted when not pregnant to a dose of only 2-5 mg.

The value and safety of hormones for inhibition of lactation seems proven. There remains only the choice of the best preparation. Here the synthetic oestrogens have the advantage of cheapness and of ease of administration. Stilboestrol was the first of these to come into general clinical use and is probably today the most widely used. Given in gradually diminishing doses over a 5-6 day period after parturition, it gives satisfactory results in a high proportion of cases, though treatment may need to be repeated. The alternative is to give an initial large dose of a synthetic oestrogen, such as hexoestrol dipropionate in oil, by injection. This has presumably a similar effect, as absorption takes place in gradually diminishing amounts over a period of 4-5 days. This may present some advantages over the twice-daily administration of tablets, though repetition of treatment may become necessary.

Whatever method is employed, success is assured in the majority of cases, and the use of hormones represents a real advance on the methods of treatment formerly employed.

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A SURVEY OF THE PLACE OF COW'S MILK IN THE HUMAN DIET AND OF THE EFFECT OF PROCESSING ON ITS NUTRITIVE VALUE

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1 Importance of milk in satisfying dietary requirements
2 Milk-fat
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Ever since the dawn of history when man first domesticated animals he has been in the custom of using their milk for food. It is significant that the carnivorous dog, probably the first animal to be tamed, was never used for this purpose; the milch animals are, with the historic exception of the nurse of Romulus and Remus, herbivorous and, but for the mare and female ass, all ruminants. This may have been largely a question of convenience and economics, as the animals kept for meat and milk did not compete with man for food, and converted into valuable foodstuffs plant-matter otherwise of little use to him. Their nutritional requirements are very different from those of men, and ruminants especially derive from the symbiotic activities of the paunch-flora essential factors which man can obtain only from the diet. The rate of development of their young also differs from that of the child. For these reasons the composition of human milk, best adapted to promote the growth of the baby, is dissimilar in many respects to that of the cow, specially suited for the nutrition of the calf. It nevertheless remains broadly true that cow's milk is probably the most perfect single food of man.

In this connexion there has been much loose thinking about the merits of cow's milk, more particularly in Britain, and there has arisen a legend crediting nature with having specifically designed this fluid for the benefit of the human race. According to this legend, any interference with the " natural state " of the milk as it leaves the udder is harmful, and its devotees condemn any form of heat-treatment and the associated evils of milk-processing. The balance of scientific proof is heavily against such views. Milk is a great improver of diets but, as will be shown later, there is no evidence to indicate that properly executed heat-treatment makes it less suitable for this purpose. Every form of processing affects to some degree one or the other of the more labile constituents of milk, but on the whole the changes are not serious. Moreover, cow's milk is only quite exceptionally taken by itself. It cannot therefore be considered on its own

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in a nutritional vacuum, but as a constituent, albeit very important, of the mixture of foods forming the normal diet of young, adult and old.

1. Importance of milk in satisfying dietary requirements

Milk is a variable product and its composition depends on many factors such as the breed of the cow, her feeding and health, the season of the year and the stage of lactation. A single set of figures such as is quoted in table I can serve only to illustrate its broad nutritive characteristics.

TABLE I. AVERAGE COMPOSITION OF 100 g. OF SUMMER MILK

Major constituents		Minerals		Vitamins	
Water	87.6 g.	Calcium	0.12 g.	A, Carotene	150 international units
Total solids	12.4 g.	Phosphorus	0.10 g.		
Protein	3.3 g.	Magnesium	0.01 g.	B_1	45 μg.
Fat	3.6 g.	Iron	0.03 g.	Riboflavin	150 μg.
Carbohydrate	4.7 g.			Nicotinic acid	80 μg.
Calories	66			B_6	70 μg.
				Biotin	2.5 μg.
				Pantothenic acid	250 μg.
				Inositol	18 mg.
				C	2 mg.
				D	2 international units

Man has developed successful dietary patterns from which milk is almost entirely excluded but, on the whole, superior physique and the mental attributes associated with robust health are more commonly found in those civilizations where it is plentifully used. Significantly, too, in communities whose food contains little or no milk, especially in the more primitive though healthier communities, breast-feeding is often prolonged into the second and even third year of the child's life.

It is generally agreed that the importance of milk as food is due mainly to its content of protein of high biological value, its exceptional richness in calcium, and its generous supply of preformed vitamin A, and of riboflavin and other members of the vitamin B complex. The characteristic carbohydrate, milk-sugar, doubtless exerts a beneficial effect on the flora and hydrogen-ion concentration of the gut of children and probably of adults. The large amount of finely-dispersed and well-assimilable fat is a further asset.

The nutritional contribution of milk may be expressed in terms of dietary requirements. Several such yardsticks have been put forward in recent years by various authorities, the latest being that of the United States National Research Council (1945). This body has listed recommended allowances for various physiological classes. It can be calculated that one pint[1] of milk of the composition quoted in table I supplies seven-eighths of the calcium, over one-quarter of the protein (including one-half of the animal protein), slightly more than two-fifths of the riboflavin, just under one-fifth of vitamin B_1 and of the vitamin A, and one-eighth of the energy recommended for a moderately active man. A similar calculation shows that a five-year-old child can obtain from one pint of milk one-quarter of its daily needs of energy, little less than one-half of the protein (including almost all the animal protein), nearly three-quarters of the calcium, one-third of vitamin A and vitamin B_1, and three-quarters of the riboflavin allowance. It will be seen that the contribution to the needs of the child is not only larger but more evenly distributed, indicating the special value of milk for the young. It should be remembered that the american recommendations are set very high, and that lower standards, especially for certain vitamins, are doubtless compatible with adult health, and have, in fact, been officially used in Britain (Combined Food Board, 1944).

Other protective foods, notably eggs and liver, are in some respects equal or superior to milk, yet none of them achieves that balance of nutritive properties which makes the latter probably the most valuable single food of man. For one thing, apart from its high content of valuable nutrients, milk is also consumed, or potentially available, in larger quantities; though it contains for example much less riboflavin than an equal weight of liver, it is in the USA the most important single source of this factor (Cheldelin & Williams, 1943). The supply of milk, and of eggs for that matter, is much more elastic than that of liver; it takes one ox to provide one liver.

The position is similar with vitamin A. Liver is much richer in it than milk, yet milk is by far the more important source. According to Virtanen (1938), milk and milk-products are the main sources of vitamin A in finnish diets in late winter and spring and determine largely the adequacy of the vitamin-A content of the diet.

The concentration of vitamin B_1 in milk is moderate, and it is perhaps surprising that, before the introduction of enriched bread, it was in the USA the second best source of this vitamin in the diet (Lane, Johnson & Williams, 1942).

As a source of vitamin C, milk is seldom considered at all, yet the amount of vitamin C originally secreted into it is, in the USA, equal to that supplied by the citrus crop of that country (Sharp, Guthrie & Hand, 1940). Even in Britain, the 1,000 million gallons drunk every year could supply the consumers with 90 tons of ascorbic acid. In fact, owing to the effect of exposure to light (Kon & Watson, 1936) and of handling (Sharp *et al.* 1940; Mawson & Kon, 1945) only a fraction of these amounts is present in the milk as it reaches the table.

2. Milk-Fat

A lively controversy, almost entirely based on experiments with rats, has recently been going on about the nutritive value of milk-fat, for which superiority over other edible fats was claimed by some workers and denied by others (the literature up to 1945 is reviewed by Henry, Kon, Hilditch & Meara, 1945; cf. also Cowgill, 1945). The latest suggestion is that vaccenic acid, an isomeride of oleic acid, is responsible for the superiority of butter (Boer, Jansen & Kentie, 1946; Brouwer & Jonker-Scheffener, 1946), but the chemical and biological proof

[1] [1 pint = 0.568 l.—Ed.]

is not yet entirely convincing. Whether these supposed special properties of milk-fat, even if finally proven, are likely to be of importance in human nutrition is, to say the least, doubtful (Council on Foods and Nutrition, 1942).

Quite apart from modern considerations of nutritive value, cream has proverbially and since time immemorial been regarded as the most valuable part of milk, and milk from which the fat has been removed has borne a stigma of inferiority. This prejudice still persists but in fact skim milk, so convenient to use in the dry form, is a most valuable food, deprived it is true of vitamin A by the removal of fat, but with all other nutritionally-important constituents of milk proportionately increased. It is naturally unsuitable as a food for babies, and in Britain it must be clearly labelled as unsuitable.

3. Milk as a Dietary Supplement

Except by the artificially-fed baby, cow's milk is seldom taken alone, and it is in its ability to supplement other foods in a mixed diet that its chief value lies. It blends, for example, most efficiently with such staple foods as cereals and potatoes. It may truly be said that on this property of milk to improve and ennoble other foods, to add to them various essentials, rests the foundation of the modern knowledge of nutrition forged in the laboratories of Hopkins, of Osborne and Mendel, and of McCollum. Even though one should be cautious in reasoning from mice to men, one cannot help being impressed by the results of Campbell & Sherman (1945), who raised 59 generations of rats in health and vigour on a diet consisting solely of a mixture of five parts whole wheat and one part dried milk with some table-salt, and distilled water to drink.

This enhancing effect is largely due to the contribution of calcium, vitamin A, and vitamins of the B_2 complex, and also to the marked supplementary relationship between the proteins of milk and those of other foods (cf. Mitchell & Hamilton, 1929; Block & Mitchell, 1946).

It may prove useful to consider at this stage the changes in the nutritive value of milk caused by the various commercial methods of preservation, and to examine then how milk in its several forms fits into the patterns of human nutrition.

4. Pasteurized Milk

This process, in which pathogenic, and most other, organisms are killed by the application of heat well below the boiling-point of water, is usually done by the holder or by the High-Temperature : Short-Time (HTST) method. In the former, the milk is held for ½-hour at 145-150°F,[1] in the latter for a matter of seconds only at a temperature of not less than 162°F. Exhaustive experiments carried out some 10 years ago in Britain (Milk Nutrition Committee, 1937; Houston, Kon & Thompson, 1940) and since largely confirmed (cf. reviews by Kon, 1938b, 1940, 1943) have shown that in holder-pasteurization there is a loss of some 10 % of vitamin B_1 and 20 % of vitamin C, but no loss of riboflavin or of vitamin A and carotene. The availability of calcium and the biological value and digestibility of the milk-proteins are also not affected. More recently Hodson (1944, 1945) and Lawrence, Herrington & Maynard (1946) found that nicotinic acid, biotin and pantothenic acid also survive pasteurization without loss. There are, on the other hand, indications that vitamin E is affected (Anderson, Elvehjem & Gonce, 1940). It may be added that calf-feeding experiments carried out in Britain (Milk Nutrition Committee, 1938b) did not disclose any significant effects of holder-pasteurization on the nutritive value of milk.

The treatment is not alone to blame for the damage to vitamin C; milk which had never been exposed to light or contaminated with copper is unaffected. It is only the more labile form of the vitamin, reversibly oxidized under the action of light, which is destroyed, while reduced ascorbic acid itself, the form in which the vitamin is secreted by the normal cow, is not altered (Kon & Watson, 1936).

In a study of the vitamin-C content of milk as consumed, Mawson & Kon (1945) found that on reaching the table pasteurized milk had only one-half of the amount of vitamin C present at this stage in raw milk. There is little doubt that this difference was only partly due to heat-treatment itself; the pasteurized milk was probably handled more than the raw and, because of better keeping-quality, was delivered less promptly.

Riboflavin is also affected by light: in fact, it is the substance that sensitizes ascorbic acid to photo-oxidation (Hopkins, 1937, 1938; Hand, Guthrie & Sharp, 1938). Exposure of milk to sunshine in pint or two-pint delivery-bottles may cause serious losses of this vitamin (Peterson, Haig & Shaw, 1944; Ziegler, 1944).

It is generally agreed that the HTST method of pasteurization is even less injurious than the holder method, though most of the evidence rests on the measurement of vitamin C only (cf. Kon 1940, 1943; Mawson & Kon, 1945). Holmes, Lindquist, Jones & Wertz (1945) compared the two methods directly and found no loss in the former of riboflavin, vitamin B_1 and vitamin C; with the latter, 18 % of vitamin C and 9-20 % of vitamin B_1 was lost. With a method of HTST pasteurization during which milk was to some extent exposed to light, Ziegler & Keevil (1944) observed losses of riboflavin amounting to 9-16 %.

5. Sterilized Milk

Sterilized milk is popular in some large British towns, especially London and in the Midlands, because of its excellent keeping-quality. A study of this milk at Shinfield (Kon & Henry, 1938; Henry & Kon, 1938a, 1938b, 1938c; Henry, Ikin & Kon, 1938a, 1938b; Gillam, Henry, Kon & White, 1938; Kon, 1938a; Houston *et al.* 1940) showed that the drastic heat-treatment destroys about half the vitamin C and 30-50 % of vitamin B_1, and that the biological value of the proteins is also affected, though to only a slight extent.

6. Condensed Milk

The kind of condensed milk generally known as "evaporated" is sterilized by heat at a temperature of 240°F. after partial removal *in vacuo* of the water, whereas in sweetened condensed milk bacteriological purity is achieved by the addition of cane-sugar which checks bacterial growth, and exposure to high temperatures is

[1] [t°F. = 5/9(t-32)°C.—Ed.]

avoided. It is clear that the processing of the unsweetened milk is more injurious to the labile nutritive factors than the manufacture of the sweetened variety. Evaporated milk loses some 60 % of the vitamin C and 30-50 % of the vitamin B_1 originally present (Henry, Houston, Kon & Osborne, 1939; Henry, Houston, Kon & Thompson, 1944); vitamin B_6, nicotinic acid, pantothenic acid, choline and biotin are, however, not affected (Hodson, 1944, 1945).

In contrast, sweetened condensed milk may contain only some 10 % less vitamin C and 5 % less vitamin B_1 than the equivalent quantity of raw milk from which it was made (Henry *et al.* 1944). It is of interest that as long as 25 years ago Hume (1921) noticed that sweetened condensed milk was a good source of vitamin C.

Tins of condensed milk will keep for an appreciable time, though the palatability gradually deteriorates and vitamins C and B_1 suffer progressive loss (Henry *et al.* 1939, 1944; Knott, 1942). It should be pointed out that sweetened condensed skim milk may be highly dangerous if wrongly used. The unscrupulous sale in the tropics of this product, "ideal for producing in bottle-fed infants a vitamin A deficiency" (Meulemans & de Haas, 1938), has led to many tragedies; it was responsible for two-thirds of all cases of xerophthalmia observed in a Batavia hospital in infants up to 2 years of age (de Haas, Posthuma & Meulemans, 1940).

7. Dried Milk

The two main methods of preparing milk as free from water as possible are spray- and roller-drying. With high-class products there is not much to choose nutritionally between these two processes, and their effects are no more detrimental than those of holder-pasteurization with the exception that the biological value of the proteins is slightly reduced by the drying (Henry *et al.* 1939; Fairbanks & Mitchell, 1935). Full-cream dried milks deteriorate rapidly on storage in the presence of air, because of oxidative changes in the fat, but they can be kept for a long time hermetically sealed in an atmosphere of inert gas such as nitrogen or carbon dioxide. If, however, the temperature to which milk is preheated before drying is raised from the usual 165°F. to 190°F., powders so produced are much more resistant to oxidation when exposed to air because of the formation of sulphydryl compounds which act as antioxidants, and the more complete destruction of oxidizing enzymes. The higher temperature of preheating is no more deleterious to the labile vitamins than the lower one, the stability on storage in air- or gas-pack of vitamin A and carotenoids and of vitamin C is enhanced, and the keeping-quality of the gas-packed milk is remarkable (Mattick, Hiscox, Crossley, Lea, Findlay, Smith, Thompson, Kon & Egdell, 1945). The biological value of the proteins of dried milk preheated to 190°F. does not differ from that of milk dried after preheating to the lower temperature (Henry & Kon, 1947b).

Dried skim milk is much less prone to oxidative changes and can be stored in the presence of air for long periods of time without loss of nutritive value, provided that its moisture-content is below 3 %. If this is higher, the biological value of the proteins deteriorates, as lysine gradually becomes unavailable by combining with lactose (Henry, Kon, Lea, Smith & White, 1946).

The concentrated stable forms of milk are usually manufactured when cows are on pasture and milk is plentiful. Despite some losses caused by the treatment, such milk may actually be nutritionally superior to fresh winter-milk from stall-fed cows. In general it may be said that the normally-occurring fluctuations in the compositional quality of milk exceed in magnitude the changes due to properly executed heat-treatment.

8. Observations and Experiments with Children

There is much evidence in human nutrition of the value of milk as an improver of diets, especially for children, and only a few examples can be quoted here. Naturally, the poorer the original diet, the more obvious the beneficial effect. For example, the addition of 1 quart (american, 946 ml.) of milk to the diet of negro children in an orphanage in which severe malnutrition existed was followed by spectacular improvement of the milk-drinkers, and later, of the control children when they were also given the benefit of the addition (McCollum, 1924). Aykroyd, Krishnan & Madhava (1937) and Krishnan & Mitra (1938) obtained statistically-significant improvements in height and weight and marked improvements in general condition in relatively small groups of children receiving in addition to a typical south-indian diet the equivalent of 1 ounce[3] of dried skim milk daily, when compared with similar groups of children receiving a supplement of equal caloric value of millet or of ordinary biscuit. Equally striking evidence is available from New Zealand with Maori children (Turbott & Roland, 1931), Japan (cf. Kon, 1934), Malaya (Scharff & Sinnadorai, 1937), the Philippine Islands (Concepcion & Paulino, 1938, Bulatao, 1938), the Nyasaland Protectorate (1938) and North Borneo (cf. *Nutr. Abstr. Rev.* 1939, **8**, 839).

Probably the most detailed experiments on the value of milk for the growing child have been carried out in Britain. Some of them were planned to investigate the nutritive effects of heat-treatment, a problem which attracted here much attention. Corry Mann (1939) has recently reviewed the results of his early work done over 35 years ago on the addition of milk to the diet of children in poor circumstances living in institutions. In one comparison, twenty children receiving the institutional diet alone gained in 12 months 3.75 pounds[4] in weight and 1½ inch[5] in height, while the corresponding gains for twenty children who received a daily addition of 2 pints of raw milk were 5.5 pounds and 2⅛ inches respectively. At that time the bacteriological quality of the milk was very low, and there were many instances of milk-borne infection among the children receiving it. In another similar experiment, twenty control children gained 3.65 pounds and 1½ inches and twenty children given in addition 1 pint of flash-pasteurized milk showed increments of 5.75 pounds and 2½ inches. No infective disturbances were observed on this occasion.

Ten years later, Corry Mann (1926) carried out further experiments in a colony of boys in the vicinity of London, and with groups of 20-40 children found that the addition to the diet of 1 pint of milk produced better gains in weight and height during one year than equicaloric

[3] [1 ounce = 28 g.—Ed.]
[4] [1 pound = 0.454 kg.—Ed.]
[5] [1 inch = 2.54 cm.—Ed.]

supplements of vegetables, margarine, butter and sugar or additions of watercress and casein.

A few years later, large-scale experiments with over a thousand children were carried out in Scotland under the aegis of the Scottish Board of Health (Orr, 1928; Leighton & Clark, 1929). In each of seven centres, four groups of schoolchildren were selected to receive (*a*) whole milk, (*b*) separated milk, (*c*) a biscuit ration of the same caloric value as the separated milk, and (*d*) no addition to their usual diet. The quantity of milk varied from ¾ to 1 pint according to age. The experiments lasted 2 years, and showed the superiority of the diets supplemented with the two kinds of milk over the other two treatments. There was no indication of any marked superiority of the whole-milk supplement over the addition of separated milk.

Later still Leighton & McKinlay (1930) carried out, also in Scotland, their well-known experiments. For 4 months in certain schools in Lanarkshire, 5,000 children were given daily ¾ pint of raw milk, and 5,000 children in these same schools were used as controls. In a different set of schools 5,000 children received ¾ pint of milk from the same source but pasteurized, and another 5,000 in these schools acted as controls. The conclusion of the authors that, while their experiment had demonstrated the beneficial effect of the addition of milk, it had shown no difference in this respect between raw and pasteurized milk, was challenged by Bartlett (1931) and Fisher & Bartlett (1931), examined critically by "Student" (1931) and supported by Elderton (1933); "Student", however, expressed doubts as to the validity of her evidence (cf. Kon, 1934). It seems safe to conclude that the value of milk to growing children was definitely proved, but that the original defect of the experiment, the trying of the two milks in different schools which may not have been chosen at random, makes it impossible to decide whether there was any difference between raw and pasteurized milk.

A few years later, another large-scale experiment was planned by the Milk Nutrition Committee (1938a, 1939). 8,000 schoolchildren from Luton, Wolverhampton, Huddersfield, Burton and Renfrewshire were randomly divided into four groups: a control group receiving a small amount of biscuit as a *placebo*, another group receiving ⅓ pint of pasteurized milk, and two groups receiving respectively ⅔ pint of raw and of pasteurized milk. The treated milk was from the same bulk as the raw. The observation lasted one year, and 6,000 children were present at all medical examinations. It was found that the supplements of milk brought about definite improvement in physique, in general appearance and in scholastic ability and, to a lesser extent, in muscular strength. Two-thirds of a pint produced more marked effects than ⅓ pint, but the differences between raw and pasteurized milk were negligible.

It is noteworthy that the effects of the additions of milk have been progressively less striking in the succeeding tests just described. It seems likely that the undoubted general improvement in the diet of the people was mainly responsible for this change. The improvement meant not only that the diets were on the whole more adequate, but that they contained more milk, and it stands to reason that by the law of diminishing returns further additions of milk produced less effect.

Quotations from the vast body of evidence on the value of milk in the nutrition of the child can be multiplied almost at will. The findings in Britain are fully confirmed by american experience. Of the numerous studies there those of Lininger (1933) and of Roberts, Blair, Lenning & Scott (1938), MacNair & Roberts (1938) and Roberts, Englebrecht, Blair, Williams & Scott (1938) may be quoted as examples.

9. Specific Effects on the Child

Evidence is also available of more specific effects of milk in the diet of the growing child, especially its intimate connexion, at any rate with dietaries of the european type, with the building of bone (Sherman & Hawley, 1922; Outhouse, Kinsman, Sheldon, Twomey, Smith & Mitchell, 1939; Kinsman, Sheldon, Jensen, Bernds, Outhouse & Mitchell, 1939; Macy, 1942), and with the development of normal teeth resistant to caries (Mellanby, 1934).

While laboratory experiments have shown that the effects of properly performed heat-treatment are not on the whole severe, experiments and observations with children make it clear that in practical nutrition the changes, whatever they are, are without any consequence. Much of the evidence about raw and pasteurized milk has already been reviewed above. The equally negative findings of Frank, Clark, Haskell, Miller, Moss & Thomas (1932) in the USA may now be added. Though direct comparison in human experiments of other forms of heat-treated or processed milk with raw milk are fewer, they are consistent in showing no ill effects of these procedures. For example, Graham & Morris (1937) found no difference in retention by five children of calcium, phosphorus and nitrogen from raw milk or from the same milk boiled. This confirmed their earlier experience with infants (Morris & Graham, 1933). Steggerda & Mitchell (1941) showed that the commercial drying of milk did not decrease the availability of its calcium for the adult. Evaporated milk is generally accepted as very satisfactory in infant-feeding, while in metabolic experiments with children Souders, Hunscher, Hummel & Macy (1939) actually obtained better retention of nitrogen and calcium from evaporated than from liquid milk.

10. Milk and National Nutrition

In the years immediately preceding the last war, there was increasing realization by governments and responsible bodies throughout the world that the diet of countless millions was inadequate in kind and often in quantity. In this field the Health Organisation of the League of Nations, by virile and inspired leadership, achieved successes denied in other spheres to the main body of that Society. Publications of the League prepared by leading experts dealt with the improvement of mass nutrition and especially with the raising of the dietary level of the physiologically-vulnerable classes: children, adolescents and pregnant and lactating women. The value of milk in this connexion has been exhaustively considered by the League (League of Nations, 1936a, 1936b, 1936c, 1936d, 1937, 1938; League of Nations Health Organisation, 1936, 1938; Bendixen, Blink, Drummond, Leroy & Wilson, 1937; McDougall, 1939a, 1939b) and dietary patterns have been suggested for children which included 1,000 g. (1¾ pints) of milk daily. In more recent years a liberal allowance has been endorsed by the United States National Research Council (1945) which recommends more than one (american) pint of milk, while

in Britain the essential need of children for milk was recognized during the war by the priority allowance under the *National Milk Scheme* of 1 pint of milk daily to all children under five and of ½ pint daily to children and adolescents between five and eighteen ; these have also the benefit of the *Milk in Schools Scheme*. The efficacy of this measure may perhaps best be gauged by the statement of the Chief Medical Officer of the Ministry of Health in his review[6] on the state of public health during six years of war (Ministry of Health, 1946) that " The national provision of milk and vitamin supplements to the priority groups has probably done more than any other single factor to promote the health of expectant mothers and young children during the war . . . "

11. Milk in the Adult Diet

That milk is a valuable addition to the diet of the adult is hardly open to question, but it would be difficult to quote definite scientific proof of its value for the adult male or the quiescent female, though much indirect evidence, like that of the classic study of Orr & Gilks (1931) of the health of two african tribes, is available.

It is, however, in the nutrition of the pregnant, and especially the lactating, woman that milk is of paramount importance. The development of the child in the womb and, to an even greater extent, the secretion of breast-milk, place on the expectant or lactating mother demands for calcium and other minerals, for protein and vitamins, which milk is best suited to satisfy. Her exceptional needs are recognized by the allowance of 1¾ pints of milk daily in the League of Nations' (1936b) dietary scheme. Milk-rationing in Britain allows the expectant mother 1 pint of milk daily in addition to her ordinary adult allowance, and a similar quantity to mothers of babies under 1 year, which means that a mother who is breast-feeding may obtain 2 pints a day for herself.

There is ample evidence from animal experiments, and from observation on man, of the progressive demineralization of the skeleton in old age (McCay, Crowell & Maynard, 1935 ; Meulengracht, 1938 ; Todd, 1942 ; Stare, 1943). The experiments of Henry & Kon (1947a) have shown that, with the rat at any rate, the process can be stopped by raising the level, and thus increasing the potential, of the bone-minerals in the diet. It is established that a good supply of calcium is advantageous for the growing animal or child. It is less certain whether maintenance of calcium equilibrium in advanced age is equally desirable. In senility, calcium tends to be deposited in tissues other than the bone, and a more generous intake might possibly contribute directly to this aberrant calcification. It may be, however, that this is a direct result of the bone-atrophy, as in the mobilization of bone-salts in intoxication with vitamin D. If that were true, the damming of bone-katabolism by increased supply of calcium and phosphorus in the diet might well prove beneficial, and milk would be an ideal source of these elements in old age. To put it cynically, the second childhood deserves perhaps the same sort of priority for milk as the first.

[6] [An account of this report by the Chief Medical Officer will be found in *BMB* **1030**.—Ed.]

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NUTRITIONAL COMPARISON OF HUMAN AND COW'S MILK FOR INFANT-FEEDING

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1 Criteria of optimal nutrition
2 Calories: carbohydrate and fat
3 Protein
4 Minerals: calcium, phosphorus, iron and copper
5 Fat-soluble vitamins A, D and K
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An Advisory Committee on Mothers and Young Children recently presented a report to the Minister of Health on the breast-feeding of infants (Ministry of Health, 1944). Part II of this report is concerned with " the claims upon which arguments in favour of breast feeding have, in the past, been founded ". The general arguments supporting the slogan " Breast feeding is best feeding " are : it is cleaner ; it is easier ; it is cheaper ; it is Nature's way ; breast milk is the perfect infant-food. There are psychological arguments adduced about which there is some uncertainty.

The medical arguments used in support of breast-feeding are listed under ten headings. Two are dismissed as unsupported by experts—namely, that breast-feeding produces better-shaped jaws, and that breast-feeding helps to prevent subinvolution of the uterus. Three arguments concerned with dietary deficiency-diseases in the infant are accepted by the Committee ; they agree that, provided the mother's diet is adequate, the breast-fed baby is less likely to suffer from scurvy, rickets, or iron-deficiency anaemia, than the infant fed on cow's milk alone. The five remaining arguments are largely concerned with the completely-accepted fact that breast-feeding carries far less risk of infection as compared with the use of bottles, whatever the nature of their contents.

Hence the arguments in favour of breast-feeding are elaborated to cover the fact that premature babies are more likely to survive if breast-fed, and the risk of post-operative death in, for example, pyloric stenosis, is less in the breast-fed. The whole group of infant infections—gastro-intestinal in particular—is less likely to occur in the first year of life in the breast-fed. Less tangible arguments, but probably valid in the light of experience, are that breast-fed babies are less likely to suffer from disturbances of digestion and that their general nutritional condition is more satisfactory. This last argument requires careful consideration, however. In all comparisons of breast- and bottle-feeding it is a question of " survival of the fittest ", and it is seldom that the results reported have been subjected to rigid statistical analysis. For further consideration of these medical arguments in a fair and non-technical manner, the Report should be consulted. The Committee evidently felt that a good deal more research was needed before they could be certain of their ground ; nevertheless, they open their recommendations with the statement that their report " will have made it abundantly clear that we share the anxiety to secure more breast feeding of infants ".

1. Criteria of Optimal Nutrition

There is much new knowledge of the nutrient content of human and cow's milks which is not presented in the *Report on the Breast Feeding of Infants*. Before summarizing this information, attention must be drawn to some difficulties in its interpretation. The over-riding consideration in judging the value of a dietary must be its value to the consumer in terms of health and well-being—and this consideration holds of course for infant-feeding. It is not sufficient to supply nutrients in food merely to avoid clinically-recognizable signs of malnutrition. There is undoubtedly a degree of insufficiency of supply of nutrients which may lead to a slow impairment of health which is detectable only by special investigations.

The interpretation of measurements of growth, i.e., of increase in dimensions, is also open to question ; it is not necessarily correct to assume that maximal rates of growth are optimal. The signs of optimal progress in development towards maturity may again be difficult to establish, both backwardness and precociousness being sub-optimal. Complete criteria of the value of a dietary to the infant should also take into account the possible effects of mal- or under-nutrition on health and well-being in adult life, i.e. on the quantity and quality of life. The position is therefore that criteria for optimal growth, development and performance at maturity are not available, and a firm assessment of the comparative nutritional merits of human and cow's milk for the infant must be deferred until they are established.

2. Calories : Carbohydrate and Fat

There is very little difference between the average energy-value of mature human milk and cow's milk (about 70 Cal./100 ml.). The mammary gland is very efficient in converting and secreting materials from the blood into milk. For a cow, 200 Cal. of " digestible energy " is required for each 100 Cal. in the milk (Overman & Gaines, 1933) ; there is reason to believe that the human mammary gland is even more efficient than that of the cow (Garry & Wood, 1946). At present-day prices, a human dietary in Britain costs about 1d. [£0.004] per 100 Cal., so that, assuming *no* energy to be required for mammary-gland activity, human

milk would cost 4d. per pint[1] to produce, whilst cow's milk is sold at 4½d. per pint to the ordinary consumer and at 2d. per pint (or it may be free) to mothers under the National Milk Scheme. There are however complex subsidies on foods, including cow's milk, which obscure the real costs. On the simplest basis, i.e. the cost of fodder for the dairy cow as compared with human foodstuffs, the cost of cow's milk is much less than that of human milk, even if the formation of milk in the cow is a relatively inefficient process. On the other hand, the preparation of infant-foods by technological processes is costly. Moreover, there are many instances in which no milk in any form, other than human milk, is available, and the question of the cheapest form does not arise.

More than 90 % of the Calories expended by an infant on a diet wholly of milk are derived from fat and lactose. Lactose is the sole carbohydrate of milk ; there is more of it in human milk (about 7 %) than in cow's milk (4.5 %–5 %). Its presence in the gut is known to favour the predominance of *L. acidophilus* in the gut, but it is of some interest that *L. bifidus I* is the prevailing organism in the gut-flora of the breast-fed baby. The presence of lactose in increased amounts in human milk may, by its effect on intestinal microflora, affect the amount of synthesis of various nutrients. It also promotes the absorption of calcium and phosphorus, presumably because of its influence on the hydrogen-ion concentration of the gut-contents.

There is about 3.5 % of fat in both human and cow's milk ; but it has been found recently (Hilditch & Meara, 1944) that the composition of human milk-fat differs from that of butter-fat ; in particular, the fatty acid of the former contains about 7 % linoleic acid, whereas there is little or none in cow's milk. Linoleic, linolenic, and arachidonic acids, have been shown to be indispensable for the nutrition of rats.

There is an interesting inter-relationship between fats and lactose or galactose, for the utilization of the sugars appears to be dependent on the presence in the diet of certain fatty acids. Butter-fat has in fact been shown (Boutwell, Geyer, Elvehjem & Hart, 1943) to be superior to certain vegetable oils *only* if the carbohydrate in the diet is lactose. In considering these observations, the need for the rapid synthesis of glyco- and galacto-lipids in the human infant during the first six weeks of life should be borne in mind.

3. Protein

Infants fed on cow's milk from birth have a body-nitrogen content which increases up to an age of about six months at about the same rate as it does in the foetus ; on human milk, however, the percentage of nitrogen in the body remains about the same as that at birth, and may be even lower at six months of age (Stearns, 1939). The *proportion* of the nitrogen retained from both human and cow's milk is about the same ; but the *amounts* retained on human milk are smaller (about a half, i.e. in the ratio of the amount of protein in the two milks). Infants on whole cow's milk have therefore a relatively larger store of tissue-protein than breast-fed babies, some of it occurring as muscle (Catherwood & Stearns, 1937).

Increase of protein in the infant's diet is of doubtful value if its effects can be interpreted in the light of results of increase in dietary protein for growing rats. Slonaker (1931, 1935) compared the effects of diets containing about 10, 14, 18, 22 and 26 % protein (in air-dry food). Gains in weight increased with the amount of protein in the food but, in general, performance as judged by spontaneous activity, running-distance, fertility, length of reproductive span, average number and size of litters, viability of young and length of life-span, was best for the animals on 14 % protein diet, followed by those on 10 %, and then progressively poorer as the percentage of protein increased in the diet.

By feeding a suitably-diluted cow's milk to an infant, its nitrogen-retention can be reduced so much that it equals that of a breast-fed infant. In spite of the equality of nitrogen-retention there is reduced tissue-turgor and impaired motor development in the infant on the diluted cow's milk as compared with the infant receiving more cow's milk (Jeans, 1942), the infant on human milk showing no disadvantage in its muscular development. Some factor or factors in the nature of the proteins of cow's and human milk may be concerned, and differences in the amino-acid composition of the proteins of the two milks might afford an explanation, though recent data (Williamson, 1944) do not reveal remarkable differences. In order to be able to make a comparison of the amino-acid composition at equal total-protein contents, whole cow's milk must be diluted with about an equal volume of water to contain 1.4 % casein and 0.25 % lactalbumin, whilst human milk contains 0.5 % casein and 1.0 % lactalbumin. There is more than 30 % more tryptophan in human milk than in this diluted cow's milk, but about 20 % less threonine, valine and histidine. In human milk there is three times as much cystine, but less methionine, than in the diluted cow's milk ; there is, however, not much difference between the two milks in the total sulphur-containing amino-acids (i.e. cystine+methionine). The significance of these data cannot be appreciated until we know more about the amino-acid requirements of the infant.

The foregoing evidence would provide grounds for feeding protein at a lower level than that required for maximum growth and nitrogen-retention ; on the other hand, Clements (1946a) has agreed that the protein-reserves of the infant should be maintained at the highest possible levels in order to support maximum synthesis of antibodies.

Half a century ago, Bunge drew attention to an interesting relationship between the protein-content of the milks of

TABLE I. PERCENTAGE PROTEIN IN THE WHOLE MILKS OF DIFFERENT ANIMAL SPECIES AND THE TIME IN DAYS TAKEN FOR DOUBLING THE BIRTH-WEIGHT OF OFFSPRING

Species	Protein	Days
Man	1.6	180
Cow	3.8	70(47)
Horse	2.7	60
Sheep	5.4	35(15)
Goat	3.7	22
Pig	6	14
Dog	7.5	9
Guinea-pig ...	5	7
Rabbit	14	6
Rat	12	6
Pigeon-crop "milk"	13	2

[1] [1 pint = 0.568 l.—Ed.]

various animal species and the rate of growth of offspring as measured by the time taken to double the birth-weight. Brody (1945) has recently modified and extended the data; some of his figures are reproduced in Table I. Brody remarks that the "situation is too complex for a simple generalization, although, no doubt, speed of growth, composition and physiologic age . . . of the young at birth are important factors in determining the evolutionary trend of milk composition." It might be noted here that the amounts in milk of nutrients other than protein follow somewhat similar trends.

4. Minerals: Calcium, Phosphorus, Iron and Copper

Calcium.—Cow's milk contains on the average 120 mg. calcium per 100 ml. milk—about four times as much as human milk; the concentration in both varies considerably with the nature of the diet. As with nitrogen-concentration in the body of the infant after birth, that of calcium differs with feeding with the two milks. For both, however, there is a decrease for some weeks after birth; the infant on human milk may not regain its calcium-concentration at birth until it is one year old. There is more efficient absorption of calcium from human milk, but the total amount supplied in cow's milk is so much greater, that the infant retains as much if not more calcium from the latter as from human milk. The linear growth of infants on a standardized cow's milk preparation is related to the amount of calcium retained (Jeans, 1942). The breast-fed baby, however, has an excellent linear growth at a much lower calcium-retention, and grows at a definitely greater rate than the artificially-fed baby with the same calcium-retention. We agree with the following recent comment (Macy, Williams, Pratt & Hamil, 1945) on these observations:—

> "No one knows whether the biggest baby, or the one who stores the most calcium, has a greater advantage throughout life than the infant fed breast milk, who may grow more slowly but with greater nutritional stability and may extend that steady growth farther into childhood. Indeed, studies of animals indicate that years may be added to the life span and life to the years by giving diets complete in all known dietary essentials which produce slow but steady growth."

Phosphorus.—The amount of phosphorus in human milk (15 mg./100 ml.) is only about one-sixth of that in cow's milk, but is sufficient in proportion to the amount of calcium and protein. About two-thirds of the phosphorus of cow's milk is excreted by the infant in urine.

Iron.—Human milk contains rather less, on the average, than 1 mg. of iron per 100 ml., about three times as much as cow's milk. The infant is, however, born with considerable stores of iron, and haemoglobin-levels are maintained for several months; on cow's milk, the baby's retention of iron at 3 months of age is almost negligible.

Copper.—There is about 0.25 mg. of copper per litre in human milk, and much less in cow's milk, so that the latter in respect of both the minerals concerned in haematopoiesis is inferior to breast-milk.

5. Fat-soluble Vitamins A, D and K

Vitamin A.—The vitamin-A potencies of cow's and human milk do not on the whole differ appreciably, though the proportion of preformed vitamin A to carotene is less (1 : 1) in cow's than in human (3 : 1) milk (Lawrence, Herrington & Maynard, 1945). The human-milk content of this vitamin differs according to the dietary and may be so small as to lead to xerophthalmia in the infant. The amount in cow's milk is known to vary with the type of feeding, and values of 140 and 70 international units per 100 g. may be taken (Medical Research Council, 1945) as representative of summer- and winter-milk respectively. There is no reason to believe that the amounts available in the milk of a well-nourished woman are not sufficient to meet the normal infant's requirements.

Vitamin D.—There has been much more concern about vitamin D (Mackay, 1944). It is true that infants with foetal rickets may develop in women suffering from osteomalacia due to calcium-deficiency in the diet, and that there are statements that rickets may develop in both breast- and artificially-fed babies, possibly more commonly in the latter. The vitamin-D content varies considerably in human milk from 0.4-10 international units, and in cow's milk from 0.5-4.0. But these quantities are probably quite unrelated to the real needs of the infant, which might be expected under natural conditions to synthesize part, at any rate, of its vitamin D in (or on) the skin during exposure to sunshine. At the present time, we must agree in the light of our remarks above that "without more knowledge of the proper balance of the nutrients we should not do everything in our power to increase the rate of growth of babies and then complain that this rapid rate of growth brings them to the verge of rickets" (Garry & Wood, 1946).

Vitamin K.—One view about vitamin K is that sufficient is present at birth to last the infant until it synthesizes sufficient microbially in its own intestine to supply its further needs; the other, that the supply to the foetus is determined by the amount derived by its mother from her diet (Clements, 1946b). In the latter event, if the mother eats reasonable amounts of green vegetables, then the infant will be born with adequate supplies, and its further immediate requirements of about 1 microgram daily may be supplied from 30-60 ml. of milk.

6. B Vitamins

The amounts of certain B vitamins in mature human and cow's milk have been summarized recently (Lawrence *et al.* 1945) and are reproduced in table II. There is again considerable variation in the content of human milk of some of these nutrients, depending on the diet of the mother. It has been known for many years (Andrews, 1912), for example, that the milk of mothers whose infants had died from beriberi would produce beriberi in puppies suckled by these women. There are also variations in the B-vitamin

TABLE II. B-VITAMIN CONTENT (MICROGRAMS) OF FRESH MATURE HUMAN AND COW'S MILK

	Mature human milk	Cow's milk
Vitamin B_1	14	38
Riboflavin	37	200
Nicotinic acid	183	85
Pantothenic acid	246	350
Pyridoxin	4	67
Biotin	0.8	3
Inositol	33,000	18,000
Folic acid	45	5

content of different cows' milks ; on the whole, the variations are not so pronounced as in human milk, probably due to the contribution of B-vitamins from microbial activity in the cow's alimentary canal. Some of the differences in individual B-vitamin content between cow's and human milk are considerable.

The amounts of each available to the infant should obviously be considered in relation to its requirements ; in doing so, some authorities, having accepted recommended allowances, have argued that the amounts of some B vitamins obtained from the mother's milk in breast-feeding are inadequate. The bases of requirements for B vitamins for the infant are generally not sufficiently well-founded to justify dogmatism on this point. It is, however, important to recognize the need for a balanced supply of the B vitamins. Richards (1945), for example, has shown that the administration to animals of relatively large amounts of a single member of the B-vitamin complex may induce signs of insufficiency of other members of the complex—at any rate in the offspring of the mothers to which the unbalanced mixture has been fed.

7. Vitamin C (ascorbic acid)

Cow's milk, which on the average at milking contains 2 mg./100 ml. of ascorbic acid, is a much poorer source of vitamin C than mature human milk, which contains about 5 mg./100 ml. The amounts in human milk are higher in the earliest days of lactation and may vary seasonally, or otherwise, in relation to the amount of vitamin C in the mother's diet. The infant normally is born with substantial stores of ascorbic acid. It is generally conceded that there is ample ascorbic acid in human milk from properly-nourished mothers.

8. Amount and Composition of Human Milk

Given an adequate diet, the composition of human milk does not after the early days vary much throughout lactation. If there is insufficiency of proteins, fats or carbohydrates in the mother's diet, then the usual response is a reduction in the amount of milk secreted ; shortage of vitamins in the diet leads to a reduced concentration in the milk, whilst shortage of minerals may lead to a drain on the mother's reserves. From this knowledge, the correct inference is that to maintain the quantity and quality of human milk the mother must be adequately fed—and watered ! This provision, in so far as lactation is concerned, should apply to the period of pregnancy for ample mammary-gland formation, and generally in preparation for lactation, as well as to provide flesh which may, in the interests of the infant, be milked-off during lactation.

9. Balance of Nutrients in Human Milk

Evidence is accumulating of the great importance of a proper balance of nutrients in the diet for optimal digestion, absorption and utilization ; for example, of the importance of amino-acids for absorption of calcium and possibly also of phosphorus, of phosphate for absorption of carbohydrates and possibly of fats, of vitamin D for absorption of calcium and phosphorus, and of the inter-relationship of the absorption of iron and calcium. The effect of lactose on the nutritive value of fats, and possibly in other connexions has been mentioned above. There is a close inter-relationship in metabolism, particularly in the liver, between B vitamins, some amino-acids and other metabolites. There is no doubt, too, of the superior nutritive value of dietary proteins having an amino-acid composition matched to the body's needs. All this evidence points to the need for as great a concern about the balance of nutrients in the infant's food as of the actual amount of any one nutrient.

In the past, preoccupation with increasing rates of one of the elements of growth, for example, of weight, by dietary means, may have led to competition in the body for nutrients, with detriment to the balanced achievement of the infant's genetic potentialities. It is of interest in this connexion to draw attention to the prevailing concept that the normal infant is born with stores of iron sufficient for it to maintain haemoglobin-formation for six months, whereas rate of increase at birth of calcium- and nitrogen-concentration is rather regarded as a pace which ought to be maintained after birth.

10. Supplementary and Mixed Feeding

It would seem that there are no good reasons for giving single-nutrient supplements to breast-fed infants, with the possible exception of vitamin D where appropriate radiation of the infant is not feasible. The procedure of choice is to supply an adequate diet to the mother, and supplementary feeding of the infant should ideally be such as to maintain a balance of nutrients similar to that of milk from the breast of a healthy, well-nourished woman. Such supplementary feeding would in a sense be mixed feeding.

Mixed feeding has been regarded in Britain as a preparation for weaning of the infant from the breast. The tendency in recent years has been to reduce the age at which mixed feeding is begun ; at the same time, there is an associated tendency to reduce the period of breast-feeding. It is a common feature in many parts of the world (Platt & Gin, 1938) to begin some form of mixed feeding at a very early age, and to continue breast-feeding beyond one year, sometimes as long as five years. The main supplementary foodstuff is a cereal gruel or " pap ", though small amounts of a variety of foodstuffs are also given to the infant. There appear to be no good reasons why these practices should be impugned ; on the contrary, the early employment of cereals in mixed feeding may be valuable " training " for an infant whose diet in later life will be largely based on cereal-grain products and, in the absence of supplies of other mammalian milks, it is clearly desirable to continue breast-feeding provided that the mother is adequately fed.

11. Conclusions

There are good reasons for favouring human milk as against cow's milk as a basis for infant-feeding. The importance of the balance of all the nutrients, as well as the content of individual nutrients, in the infant's diet should be appreciated. It is not possible precisely to relate the supply of nutrients to the infant's requirements, since the latter are not well-established. Single elements of growth and development cannot be accepted as criteria of adequacy

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INCIDENCE, CAUSES, AND PREVENTION OF FAILURE OF BREAST-FEEDING

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2 Production and removal of milk
3 How does the baby obtain the milk?
4 Hindrances to effective removal
5 Prevention of failure
References

No reliable statistics exist which allow us to compare the proportion of women who feed their babies at the breast today, and the length of time they continue to do so, with, say, fifty years ago. It is estimated that at the present time not more than half the babies born in Britain are breast-fed for longer than 3 months, and that by 6 months the proportion has fallen to 40 %. Whenever these low figures are mentioned, the question arises of the extent to which a true inability and a mere unwillingness are responsible. Many hold strongly that unwillingness is largely to blame, but the evidence for this view is not very convincing and is seldom reduced to statistical terms.

Unwillingness may well find freer expression than formerly, now that the risks of artificial feeding have been so greatly reduced. For over 30 years there has been in Britain no serious epidemic of summer diarrhoea such as used to claim its victims by tens of thousands in every hot season. Its dread reputation has faded from women's minds, and with it has gone the strong incentive to keep their infants breast-fed at all costs as their only real safeguard. The great fall in the birthrate and the reduction of, at least, abject poverty have had a similar influence, since the cost of artificial feeding is proportionately a much less severe drain on the family income than it was a generation ago. I do not myself meet frank unwillingness at all often, and put its frequency lower than do some observers. On the other hand I have no doubt that the fear that a child is undernourished at the breast is a very common reason for substituting bottle-feeding. The fear may be groundless, though by no means always so, and the motive, which in reality was anxiety, is easily mistaken for unwillingness.

1. Failure in the First Three Months

So much of the security of breast-feeding depends on events during the early days of milk-secretion that the factors held to be responsible for failure with which this paper will deal are centred on that period. The views put forward have been mainly derived from clinical studies made at a maternity hospital and at infant-welfare centres in south and east London. No attempt is made to discuss failures in the later months, partly for reasons of space, but mainly because the earlier the deprivation of human milk the greater the risk to infant life. We have seen that five out of six failures have occurred by the end of the third month, and in my experience a high proportion of these have already taken place by the sixth week or soon after, and many are directly traceable to influences in the first fortnight.

Now, if anything unfavourable to success should gain entry, however unwittingly, into the management of breast-feeding during the lying-in period, and especially should it become incorporated in the teaching of training-schools for nurses and midwives, its effects may become disastrously widespread. The danger is increased by the large number of women now confined in hospitals. A generation ago, rather less than one-twelfth of all

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NUTRITIONAL COMPARISON OF COW'S AND HUMAN MILK

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of an infant dietary. With the possible exception of vitamin D, there is not a good case for supplementing the infant dietary with single nutrients ; there may be a case for early mixed feeding and prolonged breast-feeding. It is of paramount importance, in the interests of both mother and infant, that the mother be specially fed during and also for some months before lactation.

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deliveries in London took place in institutions, whereas at the outbreak of war the proportion had risen to over two-thirds. That is to say, it was eight times as high, and today it is higher still. The tendency of nursing in hospitals is always, and understandably, towards working to a timetable, and routine, like arteries, is liable to become rigid with age. If the routine can be planned to meet the needs of both aspects of breast-feeding—the physiological requirements of milk-production on the one hand, and on the other the demands of the infant for food, sleep, warmth and so on—then it can be all to the good. But it can be quite the opposite if these necessities must fit as best they can into a design arranged primarily to suit the hours of nurses and domestic staffs.

Another difficulty is the short time allotted to the puerperium and the consequent lack of observation beyond that stage which should allow the effect of methods applied in the early days after childbirth to be tested by results. For this reason I believe that not very much value can be attached to the high percentage of breast-feeding at 12 or 14 days which maternity hospitals publish. Care of the newborn has made great advance within recent years, and there is today not only more precise knowledge of its nutritional needs than ever before, but a far better appreciation also of the value of careful nursing, of provision against infection, and of many other details. The premature baby's vastly-improved chance of survival is a good illustration of improved care. It is therefore not a little disappointing that nothing comparable can be recorded by way of control over the unreliability of women's lactation; indeed, it may be doubted if anything worthy of the name of advance has occurred within the last generation.

2. Production and Removal of Milk

Full understanding of milk-production and its steady maintenance must await further light from the physiologists, but the principle of repeated and efficient emptying of the gland, so well recognized as a necessity in dairy farming, holds good for the human also. The more the child takes, the more will be produced. Sections of the gland after weaning show that the process of involution begins with distension of the alveoli by residual milk and is followed by disintegration of the secreting cells. So that we may say that if production is to be maintained, tension within the breast must be kept below the point at which the rate of secretion is reduced, and will ultimately cease, by compression of the secretory cells. Before the use of perambulators became general, and when women carried their babies, the child of the right-handed mother spent a large part of its life supported on her left arm. From this position it fed in comfort, while at the other side it was awkwardly poised. In consequence it was quite common to find feeding confined to the left breast in each lactation, and the right devoid of milk and only perhaps a third of the size of the productive side. This was of course reversed in the left-handed, but since carrying has been replaced by wheeling, one-sided feeding is seen only when one breast is drained and the other refused because of a malformed nipple.

Another example of incomplete removal arises when more milk is produced than the child can possibly drink. There is a variable factor here, not only in the size, the vigour and perhaps the maturity of the child; but also, as Engel (1941) has very convincingly shown, in the amount of secretory tissue in different women. Thus, of two young mothers in my hospital at the same time, one never yielded more than 4 ounces[1] of milk in any day throughout her stay, while the other produced a measured amount of 55 ounces 5 days after her baby was born, and her yield remained at about this level. Now, every midwife would realize that the first woman's baby needed additional milk, and would probably have the knowledge to calculate how much. But I am doubtful whether many would realize the need to remove the excess from the breasts of the second woman, or indeed how to accomplish its removal. It is often said that an excess is of little account, and that the yield soon lessens until a balance is struck between supply and demand. This is contrary to the experience of many women, who tell me that they had too much milk while they were in bed, but that it left them shortly after they got up, and it is fully confirmed by examination of the breasts. In the example mentioned, the most the baby could drink in a day was 25 ounces, or less than half of what was secreted; while its calorie-needs were fully met by 18 ounces.

The danger of high milk-tension is specially great in the early days, and may depend less on the volume than on the rate at which the milk "comes in", as when, within the space of a few hours, the breasts become full and hard, and the skin covering them tightly stretched and glistening. With a more gradual beginning, milk soon flows from the nipples, but, when the start is of this violent kind, not only is there no outflow but it may be impossible to induce any. It is usually quite easy to detect that the skin is oedematous, particularly in the areola, and it seems that what can be found on the surface involves the ducts as well and produces obstruction. The child can of course do nothing to reduce tension to a safe level, and, indeed, if put to the breasts, merely damages the nipples, which often share in the oedema. Suckling becomes a torture, and not uncommonly mastitis supervenes. In any case, unless the engorgement is quickly overcome regression sets in and within about a fortnight production has ceased and the breasts have begun to return to the resting state. A very large proportion of women who have early resort to bottle-feeding give this account of the start of lactation. Clearly, therefore, the early establishment of a free outflow and effective drainage is of great importance and demands that we should consider the mechanism of the milk's removal.

3. How does the Baby Obtain the Milk?

To watch a baby at the breast it seems obvious enough how it gets its food. We can see it suck, notice the regular action of its jaw, and both see and hear it swallow. Gunther (1945) has shown that it can exert a negative pressure of 200 mm. of mercury. And yet I believe that the impression that it is sucking the milk out is deceptive, and that the main role of suction is to draw the nipple far back into the mouth and keep it there; meanwhile the combined action of jaw, tongue and cheeks squeezes milk from the reservoirs which lie beyond the base of the nipple beneath the areola.

[1] [1 fluid ounce = 28.4 ml.—Ed.]

But the baby's share in the act of suckling cannot of itself empty the breast. The lacteal sinuses must be replenished from within the gland, and this demands of it some power of expulsion. On this point, comparative studies have thrown much light. In the dairyman's phrase, the animal "lets the milk down", and he knows that, if the fullest amount is to be milked out, he must use his hands quickly and continuously while the flow is free. The explanation of this came when Tgetgel (1926) showed that as the teats are handled there is a sudden rise of pressure within the udder. Taken in conjunction with the difference, which is revealed in fractional milking, in the fat-content of the first and last milk to be withdrawn, the conclusion seems clear that the milk within the duct-system is forced down into the large reservoirs or "cisterns", the lowest of which are situated in the teats. The rise of pressure lasts a matter of minutes only, and more recent work by Ely & Petersen (1941) makes it seem likely that it is produced by posterior-pituitary hormones acting on plain muscle around the alveoli and in the walls of the duct-system. The amount of milk usually withdrawn can be increased by about one-fifth by an injection of pitocin or pitressin. Between milking, secretion is continuous, and Hammond (1936) has suggested the most heavily fat-laden fraction is delayed in the alveoli and finest tubules, while the remainder passes down and distends the larger ducts and cisterns. He contends that some expulsive mechanism capable of driving out the contents of the finest tubules is essential. Here, then, is evidence of a very delicate reflex evoked by manipulation of the teats, but it also requires that there should be a certain accumulation of milk, that is to say, a certain level of tension within the udder. Pain and fright can inhibit the reflex, a fact so well known in dairying that a variety of means are used to quieten animals at the milking-time.

It is strange that, whereas women are well aware of this expelling mechanism, it has received little attention as a factor of value in the management of breast-feeding. It is true that, unless questioned, many do not mention it to us, though they discuss it freely among themselves. But probably the oversight arises more freely from the fact—and this applies particularly to the first lactation—that the tingling or "drawing" which accompanies the reflex, and which they call the "draught", quite often is not experienced clearly during the puerperal period. It attracts their attention only later, when they realize that it coincides with the outrush of milk which follows within a second or two after the baby draws the nipple into its mouth. The explanation of this delay, I think, must be that it takes time for the lower part of the duct-system to become stretched and able to expand to accommodate the milk secreted between feeds. Until that has taken place milk leaks from the breasts at short intervals, and in the next phase leakage is confined to one breast as the child feeds at the other. Later yet, a third stage can be defined, when the "draught" is felt but there is no overflow, the large ducts and sinuses being now able to contain what is forced into them. The rapidity with which the child then obtains the milk, and the fact that by about the 4th week women often say that the "draught" has become actually painful, suggest that the reflex becomes more powerful as feeding proceeds. Women who have previously breast-fed a baby do not have to graduate by these stages, for the stretching has already been done; they start at the third stage, and so are often aware of the "draught" by the 3rd or 4th day after delivery, feeling it almost from the start of active secretion.

Another point deserves notice. The ability of the ducts to serve the purpose of a reservoir will be aided if the skin covering the breasts is elastic and can yield as they fill. Here, as in almost every anatomical feature of this gland, wide differences exist. In some women the mammary skin is as thin as paper and there is the least amount of subcutaneous fat, in others it is thick and unyielding and a common cause of excessive tension as the milk first comes in.

The analogy of the "draught" with the reflex rise of pressure which Tgetgel demonstrated in animals is shown by the fact that it coincides with a sudden outflow, that it is of short duration lasting for some 30-45 seconds, and that analysis shows the same difference in the fat-content of the first and last milk to be withdrawn. Moreover, it is easy to show that the fat has already become diffused through the milk within the second breast while the child is feeding at the first, Waller (1943), corresponding with the change found by Crowther (1916) when the four quarters of an animal's udder are milked in turn. The breast becomes firmly conditioned to a regular feeding-interval; that is, to a certain level of milk-tension, so that many women find that the "draught" is punctually evoked when the hour arrives and without the direct stimulus of suckling. Some are so well alive to the completeness of emptying which the "draught" affords that they waken the child when, as they say, the "draught" comes in. Indeed, they rely upon the strength and regularity of the "draught" as a sign of the security of their yield, and will often describe its weakening and delay as grounds for fearing that the yield is declining. This is reflected in the child's behaviour; for the child also very quickly becomes conditioned to the easy access to milk which the "draught" affords, and feeds for just so long as the flow lasts. Failure in its punctuality will provoke a storm of protest, and a weakening of its strength leads to refusal to go to the breast.

4. Hindrances to Effective Removal

In referring to the baby's contribution towards emptying it was mentioned that it draws the nipple far back into its mouth. This must be qualified since, in many women the nipples, one or both, have failed to reach the complete stage of development which makes this possible. The inverted and the much-retracted forms are well recognized as a serious handicap, and may make feeding an impossibility; but there are many which appear to be well-enough formed, but which a simple test shows are not so and which will give difficulty. If the areola is pinched between finger and thumb just behind the base of the nipple, the action is a fair imitation of the baby's grasp. The nipple which is quite loose in its attachment to deep tissues projects in response to this test, but when any such attachment persists it retracts towards the breast. Applied to 200 primigravidae, the range of protraction of the nipple when tested by this method was found to be good in 49, moderate in 95, and poor in 56, Waller (1946). Even if we disregard the middle group, there were over one-quarter whose babies were bound to be confronted with great difficulty.

Another point revealed by the test is the position, and so the accessibility, of the lacteal sinuses, and I believe that,

with practice, one gains an impression of their size and number. If the nipple is normally developed, they lie close to its base, and colostrum is readily expressed from them. With the retracting type, they are situated farther back, and if the malformation is marked they appear to be lacking, so that pressure has to be applied to the substance of the breast itself before any colostrum can be expressed. Much variety also is revealed in the number of ducts opening on the surface. Instead of the large number of from 12 to 20 which is described as the normal, it is common to find a main central opening with only a few others, and not seldom the central one alone. When single, it may drain into the bottom of a circular depression or lie in a transverse furrow, and this last type is most often found in the inverted or much-anchored nipple, suggesting that it is part of the developmental error.

Here, then, is a hindrance to the ease with which the firstborn can feed that will militate against effective drainage and, if the figures I have given are at all representative, and not peculiar to women seen in east London, then we must expect to meet it in a high proportion in the first lactation. But to this must be added the handicap of anything which lowers the efficacy of the baby's contribution. Now the effects of labour may be so severe that for several days the baby may make only the most perfunctory efforts to feed, and improvement may be very gradual and not complete until 3-4 weeks have passed. An infant with any respiratory difficulty will sometimes sustain the effort of drinking for but a few moments at a time. The sucking-reflex of the premature infant may not be fully developed, and even the mild form of jaundice may produce a drowsiness during which little vigour is put into the act of feeding. And the list of causes of defective sucking could be much extended. In view of the number and variety of factors from the side of both mother and child which can complicate the start, I have long ceased to be able to subscribe to the opinion that breast-feeding is a simple, natural function at which almost any woman can succeed given sufficient willingness and determination. I doubt if this holds good for more than one-third of them with the firstborn. Quite half will experience difficulties varying in kind and degree; while about a fifth can hope to succeed only if they can command help of the most skilled nature for several weeks, and even so half of this last group may have to admit failure.

5. Prevention of Failure

If the problem is approached with the nature of the difficulties kept clearly in mind, there is a good deal that can be done to overcome them. We have at my hospital found two measures of great value; one in easing the baby's task, the other directed to improve the freedom of escape of the milk. The restricted range of protraction of the nipple can be much increased by a simple orthopaedic appliance. All women with this defect are supplied with a pair of glass shields which they wear during pregnancy under a well-fitting brassière. The shield has a central opening which is placed over the nipple; the brassière exerts enough pressure gradually and painlessly to force the nipple through the opening and loosen its attachment to the breast. The time for which the shields should be worn depends on the degree of the defect, and this should be estimated early in pregnancy. For most it is long enough if they are used for the last 10 weeks before term; it is not wise to start later in case of a miscalculation and the possibility of premature delivery.

The second measure is to teach women the technique of removing the milk by hand. This is often done, but I would emphasize that, to be effective, it is a skilled manoeuvre which calls for exactitude and practice. As taught at our hospital it has two components; the first a downward movement in which the hands compress the whole breast from its margin to the areola. This is repeated several times. In the second the position of the lacteal sinuses is found and they are emptied by repeated compression between the forefinger and thumb. It is taught to all in their first pregnancy and to those who have had difficulty or failure in a previous lactation, and they are instructed to practise it daily for the last 6-8 weeks before term. It has become a routine since the discovery that those who were first taught, in order to have the necessary skill when lactation started, were the least liable to suffer from engorgement. The explanation is, we believe, that the ducts are distended by the exercise, which forces colostrum through them, and the primipara thus begins her first lactation with some of the advantages of one who has already breast-fed a child. To test our impression that this procedure was of value, we carried out a controlled experiment and compared 100 who were taught in their first pregnancy with 100 who were not, both groups being treated alike in all other respects. The results showed that not only had the pupils by far the easier start in breast-feeding but that, when both groups were reviewed at six months, 83 of the 100 were still wholly feeding as against 42 of the controls. More recently, we have found that of 300 primiparae who passed consecutively through the hospital, 79 % were also successfully breast-feeding at six months.

These two procedures must be supplemented by a constant watch on milk-tension during the puerperal period, and a very delicate sense has been acquired by the nursing staff of what is safe and when safety threatens to be exceeded. Of late years, we have employed synthetic oestrogens to check the very sudden outburst of secretion that overtakes some women, and which previously we had great difficulty in controlling. It is a method[1] of great value but requires experience; we have not been able to standardize dosage, which has to be judged by each woman's reaction. It should be stopped as soon as tension begins to fall.

A very special watch is also kept for damage to the nipples. The nurses are instructed to enquire whether suckling causes pain and to encourage the mothers to admit and not to conceal it. If the least breach of the nipple's surface can be seen through a lens, feeding is withheld until it is securely healed, the milk meanwhile being expressed by hand. I am satisfied that to this we owe many years of almost complete freedom from breast-abscesses, even before we had the help of modern chemotherapy. And, though it is more difficult to prove, I believe that the course of breast-feeding is far smoother when it is free from pain, and from the apprehension of pain. From many descriptions of what women have suffered when trying to feed with broken nipples, there can be no doubt that it must interfere with the "draught" reflex.

[1] [The hormonal inhibition of lactation is discussed in this number by Dr. Josephine Barnes (*BMB* 1107).—Ed.]

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BREAST-MILK BANKS*

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1 Sources of supply
2 Situation and specifications of a bank
3 Control of donors
4 Collection of milk
5 Conservation of milk
6 Organization

The first breast-milk bank was founded in Boston, Massachusetts, in 1910. This service is still in existence and is known as the Directory of Mothers' Milk. The first centre in Europe was opened at Magdeburg in 1919. There are approximately 20 centres in Europe and in the USA and Canada respectively, and several in South America. In Great Britain at the present time there is only one centre which supplies breast-milk for use outside the hospital, namely Queen Charlotte's Hospital. Had it not been for the war, at least two similar centres would have been in operation.

The trend of opinion at the present time in the United States seems to be that expenditure on breast-milk banks is unjustified, because the preparation of cow's milk formulae has now reached such a high state of perfection as to render the provision of human milk by this means unnecessary. It is further pointed out that when human milk is used for premature infants, it must be modified. Recent work in the United States seems to suggest that premature babies do equally well on cow's milk formulae. These opinions are by no means universally held, but should be borne in mind when consideration is being given to the establishment of a breast-milk bank.

*[Note—The reader may wish to refer also to an article on "Human milk bureaux" by Dr. Joyce Wright in the *Monthly Bulletin of the Ministry of Health and the Public Health Laboratory Service* (1947, 6, 74-77). This is the text of a report to a special committee of the Medical Research Council.—ED.]

1. Sources of Supply

The question of an adequate supply of donors is of fundamental importance, and has been a matter of concern to most breast-milk banks. Most donors appear to be obtained from the poorer sections of the community, who are paid according to the amount of breast-milk given. In consequence, when times are good, the supply of donors tends to fall. A further difficulty in America is that the incidence of breast-feeding is low in many parts of the country. It is necessary to elicit the interest of doctors, midwives and nurses, as well as of the mothers themselves, if a sufficient supply of milk is to be maintained. Too much stress should not be laid on the financial benefit to mothers. They should be made to feel they are performing a social service. In this way, it may be possible to get co-operation from mothers in higher-income groups. In some areas it is customary to make contact with the mother before the baby is born. In these cases, mothers begin to supply milk before the end of the first month. In some cases mothers are registered for this purpose as late as the sixth month of the lactation-period. The mother remains on the register as long as she is lactating and her milk is of good quality and quantity. This may be for as long as eighteen months. This does not mean that the mother nurses her baby beyond the accepted period. Other centres discontinue the taking of milk at the end of the ninth month after delivery.

FAILURE OF BREAST-FEEDING

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Perhaps the most difficult problem of all is to gauge the appropriate interval between feeds. The baby's intake is found by test-weighing, and the number of feeds required in the day is calculated so as to bring the amount up to its caloric needs. Full drainage of the breasts is secured by the method described. The nurses instruct the mothers when milk should be expressed by hand, and give them such assistance as they need; for the most part they can do it without help. A long interval at night is a disadvantage which leads to the breasts becoming overfull and the baby crying with hunger. Were the staff available, I should favour most women giving a night-feed at this stage; few abstain from doing so when they return home, and I think that their lactation benefits. The length of time a baby spends at the breast is not regulated, but continues as long as it can be persuaded to drink. We do not see the bad results which are so often attributed to overfeeding and, though it is something of a heresy, I am persuaded that most babies profit by getting the milk quickly. With feeding directed in this way, some two-thirds of the mothers have a definite appreciation of the "draught" reflex before they leave hospital.

Finally, and as an instance of how drainage alone can maintain milk-secretion, the staff has much success in enabling the very premature infant to be breast-fed. The mother is retained until she is skilled in removing her milk by hand, and on her return home she sends or brings it once daily to the ward. Her infant stays in the special nursery until it reaches a weight of 4-4½ pounds[a], when the mother is re-admitted. It seldom takes more than a few days for direct feeding to be established. The average length of stay of these babies in hospital is 40 days.

[a] [1 pound = 0.454 kg.—ED.]

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2. Situation and Specifications of a Bank

The bank may be sited in a maternity or children's hospital, or in a separate building. If it is situated in a hospital, it is not considered by some authorities desirable that it should be placed in the milk-kitchen. In other institutions, breast-milk and cow's milk formulae are dealt with in the same milk-kitchen, usually at different times and with separate staff. The amount of accommodation provided varies, depending on whether the milk is collected at the mothers' own homes or at the institution. In the former case, at least four rooms are required—a waiting-room, office, refrigerator- and sterilizing-room with equipment for washing bottles, etc., together with a staff-room and sanitary accommodation. In the case of the latter, there will be required in addition a mothers' dressing-room with cubicles and possibly a nursery for the temporary accommodation of any children the mothers may bring with them, and a milk-expression room with a separate booth for each mother.

The rooms should be light and well ventilated and the walls finished with a washable paint. The floors of rooms where the milk is handled or stored should be of impervious material and easily cleaned. All furniture in these rooms should be made of material which can be scrubbed. If the milk is to be expressed at the institution, then the mothers must be given clean overalls to put on after they have removed their outdoor clothing, and caps and masks must also be provided for their use. A detailed list of the plant and equipment is given in an article on Recommended Standards for the Operation of Mothers' Milk Bureaux in the *Journal of Pediatrics* (1943, **23**, 112).

3. Control of Donors

In most cases the examination of the mothers is stringent. One or two centres think this is unnecessary as the milk is always sterilized. Precautions must be taken to see that the health of the donor's infant does not suffer, and the child should be weighed and examined at regular intervals. The health of the staff is also important and they should undergo a thorough medical examination. There should also be enquiry into the family history of the donor. In every instance, the home of the mother should be visited to get a picture of the economic situation and general hygienic conditions of the home. This initial visit must be followed by periodic home-visits by the nurse to see that good conditions are maintained.

In most centres the examination of the mother includes radiography of chest and heart, sputum-test, throat- and nose-cultures, vaginal smears and Wassermann test. This examination is carried out before the mother is accepted as a donor and also after any illness.

4. Collection of Milk

The milk may be collected at the mother's own home, at the maternity hospital, or the mother may come daily to the breast-milk bank and express it there. In some cases, the mother may be resident at a hostel attached to the bank. In their efforts to get an adequate supply of milk, some institutions use all these methods. In most cases, whether the milk is obtained at home or in the unit, strict aseptic precautions are used for the collection of the milk. Expression of the milk may be by hand or hand-pump, water-pump or electric pump. The mother must be taught not only how to express her surplus milk, but also how to do it aseptically. The average amount expressed at any one time is 15 ounces[1] but it takes a donor at least a month to reach this level. The peak is reached at three months. The amount collected daily by breast-milk banks in the United States has varied from 5 to 256 ounces. In 50 % of these banks the supply was equal to the demand, but in the rest the supply fell short. If the milk is collected centrally, then it can be dealt with immediately. If, however, it is collected from the mother's own home, then containers with ice must be supplied for the mother's own use and means for their transport must be arranged. On these visits to the home, the nurse can supervise the technique of expression.

Whether the milk is expressed at home or in the hospital, the mother should wear a clean gown of washable material and a cap to cover the hair completely, and a mask should be worn. The hands and nails must be well scrubbed, and the breast and surrounding chest areas must be thoroughly washed.

5. Conservation of Milk

After expression, the milk is immediately chilled to a temperature[2] of 40° F. and pooled. Thereafter the milk is pasteurized. During cooling, after pasteurization, the bottle should be frequently inverted to prevent butter-fat from clumping. The milk is then kept in a refrigerator at 40° F. until used. Adequate pasteurization is checked by phosphatase-test and bacterial counts. If the milk is obtained in the mother's own home, tests must also be made for dilution by water or adulteration by milk other than human. The bacterial count for the pasteurized milk should not be more than 10 colonies per cm.^{3} nor should the fat-content be less than 2.9 %.

In most instances, the available supplies are used within 24 hours. Even if not used in that time, some centres state that boiled milk keeps for a long time in an ordinary refrigerator. In most centres, however, any surplus remaining after 48 hours is preserved by one of the following methods—quick freezing, slow freezing, or fractional sterilization.

In the quick-freeze method, the milk after pasteurization is rapidly frozen in small wafers of approximately one-third of an ounce and stored in glass containers in a freezing-cabinet at a temperature of −15° F. In the slow-freeze method, the milk is frozen in units of 8-16 ounces, the freezing-time being 30-60 minutes. The hardening-compartment of an icecream-making machine may be used for the purpose. Detailed descriptions of these methods, as well as of fractional sterilization, are given in the article already referred to.

6. Organization

The organization of the breast-milk bank will depend on where it is sited and whether the milk is to be distributed outside the hospital. A medical committee should be formed to determine the policy in regard to the collection, pasteurization, storage and distribution. Especially is this necessary if it is likely that the supply will be less than

[1] [1 fluid ounce = 28.4 ml.—Ed.]
[2] [t°F. = 5/9 (t − 32)°C.—Ed.]

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ANTIBODIES IN MILK

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A Domestic Animals
1 Absorption by the young
2 Relation to globulin
B Human colostrum and milk
3 Absorption by babies
4 Rh-antibodies
References

A. DOMESTIC ANIMALS

Antibodies do not pass through the placentas of the larger domestic animals; the young depend for passive immunity —which will protect them until they develop active immunity—on antibodies in colostrum or milk. Investigators (Famulener, 1912; Little & Orcutt, 1922; Mason, Dalling & Gordon, 1930; Schneider & Szathmáry, 1938) agree that colostrum is the main source. The concentration of antibodies in colostrum, before and immediately after the young are born, approaches or exceeds that in the serum of the mother, but later it falls rapidly. The ratio of the concentration in colostrum or milk to concentration in maternal serum may fall to 1:7 at 28 hours after delivery and to 1:8 to 1:20 at 4 days. But some antibody may persist in the milk up to at least 91 days (Mason *et al.* 1930).

Antibodies from species other than that of the mother also pass into the milk. Thus, if horse-serum containing diphtheria antitoxin is injected in a ewe before lambing, the concentration of antitoxin in the colostrum may, just after lambing, be as high as in the ewe's serum. Horse-serum containing diphtheria antitoxin was injected into a ewe on the 11th day after lambing; the ratio of concentration of diphtheria antitoxin in milk on the 12th day to the concentration in the ewe's serum was about 1:70. This ewe had been immunized before lambing by injection of formalinized culture of lamb-dysentery bacillus; the ratio of concentration of lamb-dysentery antitoxin, formed by the ewe, in the milk of the 11th day, to the concentration in the ewe's serum, was 1:32 (Mason *et al.* 1930). Allowing for differences of methods of estimation, the two ratios do not differ significantly.

1. Absorption by the Young

Antibodies are found in the serum of the young shortly after ingestion of colostrum. In 3½ hours, the concentration in a lamb's serum may be about 1-10th the concentration in the ewe's serum; one day after birth, the concentration in the serum may be of the same order as in the mother's serum (Mason *et al.* 1930, Schneider & Szathmáry, 1938). If colostrum is withheld and milk, containing no antibodies, is given instead, antibodies do not appear in the serum. Calves can absorb antibodies directly from cow's serum, taken by mouth, on the first day after birth, but not on the 18th day (Smith, 1930). Mason *et al.* (1930) found that lambs could also absorb the diphtheria antitoxin of horse-serum, whether the horse-serum was injected into the ewe and secreted into the colostrum, which the lamb sucked, or given to the lamb direct by stomach-tube. But a far larger proportion of the antitoxin appeared in the lamb's serum if it was given subcutaneously than when it was given by the stomach. Lambs appear to be no longer able to absorb the antitoxin of horse-serum by the 4th day after birth; but there is evidence that calves can absorb antibodies formed by the cow and ingested in the mother's milk up to the 10th day (Mason *et al.* 1930).

2. Relation to Globulin

According to Graham, Peterson, Houchin & Turner (1938), the proteins of milk are formed mainly from the globulin of the mother's serum to form caseinogen and β-lactoglobulin[1]. The serum-globulin must be split into its constituent amino-acids and these must be rearranged. If globulin is split beyond the very earliest stages its specific properties as an antigen or, in the case of antibody globulin, as an antibody, are destroyed. But milk-globulin was shown by Wells & Osborne (1921) to be indistinguishable from serum-globulin by the anaphylactic reaction. Smith (1946a) separated two fractions which he called "immune globulin"[2] B and C from colostrum and from milk; he, also, found no difference, by the anaphylactic reaction, between this globulin and γ-globulin of cow's serum.

[1] β-lactoglobulin is the protein formerly known as lactalbumin. The term "globulin", as used in this article, does not include this fraction.
[2] The name is misleading, as it suggests that the whole of this fraction is antibody, of one sort or another, which is probably not the case.

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the demand. In that case, it is essential that an order of priority should be set up. Careful records should be kept of the health of the donor and her child, the family history, the amount of breast-milk obtained, etc.

In the United States, the cost to the agencies varies from 10 cents to 35 cents an ounce. The payment to the donor varies from 5 to 15 cents an ounce, and is often supplemented by travelling-expenses and/or a meal. The charge to the consumer is usually on a sliding scale according to financial circumstances, the highest charge being in the region of 35 cents an ounce. In very few cases is the agency self-supporting. All the others have to be subsidized in one way or another. At Queen Charlotte's Hospital donors are paid at the rate of two-pence [£0.008] an ounce. A charge of £0.5 a pint[3] is made for milk supplied for use outside the hospital. There, too, a similar difficulty is found in making the bank self-supporting.

The decision to establish a breast-milk bank must, therefore, depend on whether it is considered that the value of breast-milk to weakly infants so far surpasses that of cow's milk formulae as to justify the expenditure involved.

[3] [1 pint = 0.568 l.—ED.]

The antibodies of cow's colostrum and of milk are precipitated within the same range of concentration of sodium sulphate as are those of cow's serum. The antibodies of cow's serum may be in the γ-globulin or in the T-fraction—a globulin formed on immunization, which has a mobility between those of γ- and β-globulin. The "immune globulins" of colostrum resemble the T-fraction of serum but differ slightly from it (Smith, Greene & Bartner, 1946). The T-globulin of cow's serum appears, therefore, to pass through the mammary gland, particularly in the earliest stages of lactation, with a slight but detectable alteration.

The concentration of globulin in colostrum is much higher in the first milkings than in later samples (Crowther & Raistrick, 1916). Smith (1946a) found about 13 g. of "immune globulin" in 100 ml. of the first sample of colostrum, with less in samples taken 10 hours later. In mature milk, the concentration of "immune globulin" is much less; it may rise considerably when the cow is hyperimmunized and the concentration of antibodies increases. The amount of globulin in milk, therefore, runs roughly parallel with the concentration of antibodies.

In the serum of newborn calves, the concentration of globulin, which is precipitated in the same range of concentration of Na_2SO_4 as is that of colostrum, is very low. After ingestion of colostrum, the concentration of this globulin rises rapidly. This rise does not occur if colostrum is withheld (Orcutt & Howe, 1922). Jameson, Alvarez-Tostado & Sortor (1942) found that the serum of newborn calves contained no γ-globulin. A fraction corresponding to γ-globulin was detected at 18 hours, after the calf had suckled; by 36 hours the concentration of this fraction was as high as that of the γ-globulin of adult serum. The mobility of this fraction which appears in calves' serum during the first few days is about equal to that of the "immune globulin" of colostrum according to Smith (1946b); later the mobility falls. The globulin of serum, including antibody-globulin, is being changed continually (Schoenheimer, Ratner, Rittenberg & Heidelberger, 1942). The fall in mobility as the calf gets older may indicate the replacement of the "immune globulin" absorbed from colostrum by γ-globulin made by the calf itself.

According to Polson (1943), the serum of newborn foals contains very little β-globulin and no γ-globulin: after 5 days' suckling, the β-globulin has risen to the level found at 8 months, but the γ-globulin is still very low. This recalls that Kekwick & Record (1940) found an increase of β-globulin in the serum of horses on immunization, although other investigators have found the antibodies in the γ-globulin or in a T-fraction with a mobility between those of the β- and γ- fractions (van der Scheer, Wyckoff & Clarke, 1940).

It appears, therefore, that newborn animals of certain species can absorb parts of the globulin or colostrum and of homologous or heterologous serum with little or no change. It is known that young animals can, in time, absorb enough of the protein of food, unchanged, to sensitize them (Wells & Osborne, 1921). But this absorption of the globulins of serum and milk differs quantitatively. For the amounts needed to sensitize are a matter of milligrams; while according to Orcutt & Howe (1922), the concentration of globulin in the serum of a calf may increase by 0.8 g./100 ml. in 14½ hours if, and only if, it ingests colostrum; so that the calf must absorb some 8 g. of globulin in this time. This absorption of globulin is specific; for there is no evidence of the appearance in the serum of calves of a protein with the mobility of caseinogen (Jameson *et al.* 1942). This specific absorption is not explained by any physical properties of the globulin; for the "immune globulin" of cow's colostrum has a molecular weight of 160,000 to 190,000 and a low diffusion-constant (Smith, 1946a).

B. HUMAN COLOSTRUM AND MILK

Human placentas and those of rabbits and guinea-pigs (Bourquin, 1922) allow antibodies to pass from the maternal to the foetal circulation. As the antibodies of human serum are contained mainly in the γ-globulin, this fraction is as high in the serum of newborn babies as in the mother's serum (Longsworth, Curtis & Pembroke, 1945). Human colostrum, like that of other animals, contains more globulin than the later milk does. Few estimates have been made in the earliest samples of colostrum, when the concentration of antibodies is highest. One of the first investigators, Staubli (1906) found that the concentration of typhoid agglutinin in a sample of colostrum taken one day after delivery was considerably higher than that of the mother's serum. (Sugg 1935) found that the concentration of diphtheria antitoxin in the colostrum of a woman, who was highly immunized, was about 1/3 that in her serum. Liebling & Schmitz (1943) collected colostrum from 48 to 72 hours after delivery—that is, at a time when the concentration in the colostrum of a ewe or cow has fallen well below its maximum. They found the concentration of diphtheria antitoxin in the colostrum of 29 women who had been actively immunized was, with one exception, never more than 1/50 of the concentration in the mother's serum. Sugg found that the concentration in mature milk was 1/300 to 1/500 in the mother's serum.

3. Absorption by Babies

The concentration of antibodies in the serum of babies at birth is as high or higher than that in the mother's serum. It is, therefore, not possible to show whether the small amounts of antibodies present in the mother's milk are absorbed by the baby. There is, however, evidence that babies can absorb diphtheria antitoxin from horse-serum given by mouth (Escherich, 1897).

4. Rh-antibodies

As a human baby comes into the world provided with such antibodies as its mother can supply, which have passed the placenta, the presence of protective antibodies in milk and their absorption from the intestine is of little more than academic interest. But the presence of the harmful Rh-antibodies[a] in milk may be a serious matter. Witebsky & Heide (1943) found the titre of Rh-agglutinin in colostrum

[a] The Rh-antigen occurs in the erythrocytes of 85 % of people (Rh-positive) and is absent from the erythrocytes of the remaining 15 % (Rh-negative). The baby of an Rh-negative mother and an Rh-positive father may be Rh-positive. In this case the Rh-antigen may pass through the placenta into the mother's circulation and stimulate the formation of Rh-antibodies. These antibodies may enter the circulation of the foetus through the placenta (or, possibly, into the baby's circulation via the colostrum or milk) and cause the disease erythroblastosis foetalis, of which one of the outstanding features is lysis of the erythrocytes. Some Rh-antibodies, which are particularly harmful, and detectable only by special techniques, are called "incomplete" or "blocking" antibodies.

[For fuller accounts of the Rh factor, see *BMB* 420, 421, 872.—Ed.]

at 24 hours to be equal to that in the mother's serum. As a general rule, the concentration in later milk is lower (Langley & Stratton, 1944; Davidsohn, 1945). But concentrations equal to those in the mother's serum have been found by Fisk & Foord (1944) on the second day and by Davidsohn (1945) at a time not specified. Agglutinin has been found up to the 14th day by Langley & Stratton (1944). So far, no test has been made to detect the presence of incomplete, or blocking, antibodies, except that Gurevitch, Polishuk & Hermoni (1946), found agglutination in a specimen of colostrum taken before delivery, up to a dilution of 1:4, and conglutination up to 1:6 dilution.

Although the ratio of concentration of agglutinin in colostrum and milk to that in mother's serum may fall during the first two weeks, the actual concentration in the milk may change but little, because concentration of agglutinin in the mother's serum usually rises rapidly after delivery and reaches a peak after the 5th day. How much of the agglutinin of milk is absorbed by the baby is not known, and how far this agglutinin injures the baby is uncertain. It is generally supposed that it is harmful to keep a baby with erythroblastosis foetalis at the breast (Hooker, 1941; Levine, Burnham, Katzin & Vogel, 1941). It appears that the harm caused by the anti-Rh-antibodies is not confined to the erythrocytes; it is possible that the intestinal tract may be damaged, although antibodies are not absorbed.

Agglutinins for cells of group A and B appear in the milk, after delivery, when the group of mother and baby are incompatible, as these agglutinins rise considerably in the mother's serum during the second week after delivery (Boorman, Dodd & Mollison, 1945). The concentration of A-agglutinins in milk may be very high (Davidsohn, 1945). It appears that these antibodies may be absorbed in some cases and cause hæmolysis that begins several days after birth.

The extent to which babies can absorb antibodies is of some practical interest. It might be tested by feeding babies with colostrum from a woman, not its mother, who has a high concentration of some harmless antibody, such as typhoid agglutinin, in her serum.

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EXCRETION OF DRUGS IN MILK

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1 Nicotine
2 Sulphonamides
3 Sedative drugs
4 Purgatives
5 Other substances
6 The milk of animals
References

The excretion of drugs in milk is not an easy subject for study since the nursing mother is unwilling to lend herself for experimental observations, and the cow is too large. An opportunity exists for someone to study the excretion of drugs in the milk of the goat. There are, however, a few statements in text-books for which little evidence is quoted; thus Holt (1940) says

> "A number of drugs may be eliminated in the milk, particularly when full doses are given or after prolonged administration. Atropine, many of the opium derivatives, mercury, lead, arsenicals, salicylates, iodides, bromides, and some of the alkaloid cathartics have all been found in the milk, sometimes in sufficient quantities to produce symptoms in the nursing child."

1. Nicotine

Several workers have attempted to throw light on the question whether a nursing mother should smoke. Hatcher & Crosby (1928) found that nicotine injections (0.5 mg./kg.) suppressed the milk of a cat and of a cow, but that the milk showed only a trace of nicotine. Similarly, in a woman who began to smoke 2 days post-partum, and smoked 20-25 cigarettes daily for 6 days, secretion of milk was abundant at first but decreased rapidly during the last two days. A sample was collected with difficulty after 7 cigarettes had been smoked in 2 hours. The total amount of nicotine in the milk did not exceed 0.015 mg., though there was unquestionably a trace present. This evidence suggests that smoking reduces the milk-yield.

Emanuel (1931) likewise investigated the milk of mothers who smoked, to determine the nicotine present. After smoking 7-15 cigarettes a maximum of 0.03 mg. nicotine/litre of milk was found. Nicotine could be demonstrated in the milk 1-2 hours after smoking, but the main excretion occurred 4-5 hours later. A more detailed examination was made by Perlman & Dannenberg (1942), who observed that the concentration of nicotine found in the milk increased with the number of cigarettes smoked. For heavy smokers (11-20 cigarettes a day or more), it was as high as 0.4-0.5 mg./litre. The evidence did not suggest any connexion between the extent of smoking and the size of the milk-supply; there were, however, only 55 mothers in all. The authors say "It is our impression that the number of mothers who smoked and failed to nurse their infant successfully was no greater than in the non-smoking group in this hospital." The babies were apparently unaffected by the nicotine in the milk, even when the amount was as high as 0.75 mg./litre. All the babies of the heavy smokers gained weight, while several in the other groups lost or did not gain weight. From this, it seems clear that nicotine in the milk is not sufficient to disturb the baby of a mother who smokes, even if she smokes heavily.

2. Sulphonamides

The presence of sulphanilamide in milk was observed by Adair, Hesseltine & Hac (1938), who gave their patients a total dose of 2 or 4 g. sulphanilamide orally (Table I), and withdrew their milk at 4-hourly intervals. Among 10 who received 2 g. of the drug, the total excreted in the milk varied from 3.8 to 13.7 mg. over 3 days. Among 10 who were given 4 g., the variation was from 11.7 to 54.0 mg. The authors found that the amount of drug excreted was not related to milk-volume, and that in some patients whose urinary excretion of the drug was poor a proportionately larger amount of sulphanilamide was eliminated in the milk. The concentration of sulphanilamide in the milk was higher than that in the blood, and the drug continued to be excreted in the milk long after the amount in the blood was negligible. However, the blood-concentration represents the balance between the amount entering and the amount leaving the blood at any moment, while the milk-concentration is the accumulation of 4 hours.

TABLE I. FREE SULPHANILAMIDE (mg.) EXCRETED IN MILK

(Milk of 10 human subjects)

	1st day	2nd day	3rd day	Total
2 g.-group ...	5.18	3.31	0.57	9.06
4 g.-group ...	19.25	11.79	2.41	33.45

Similar experiments were carried out by the same authors (1939) to determine the amount of sulphanilamide excreted in milk when therapeutic concentrations were maintained in the blood for three days. They found that the amount of sulphanilamide in the milk depended on the size of the dose, but that the total amount of drug excreted over 5 days was never more than 1.6 % of the dose.

Pinto (1938) obtained results in 3 patients in whom the concentration of sulphanilamide in milk was very similar to that in the blood and not only rose, but even fell with it. The only difference was that the peak of concentration in milk occurred later than that in the blood, both of the sulphanilamide itself and of the acetylated form. When the concentration in the blood fell, that in the milk fell also, the sulphanilamide presumably diffusing back into the blood. Pinto calculates that even if the concentration in the maternal blood was maintained at 10 mg./100 ml. during the 24 hours, the maximum amount received by a baby taking 1200 ml. milk per day would not be more than 0.12 g. sulphanilamide and 0.16 g. acetylsulphanilamide.

3. Sedative drugs

The excretion of barbitone in milk was studied by Kwit & Hatcher (1935), who failed to find it after giving a dose of 10 grains (0.65 g.); their method was sufficiently sensitive to detect 1 part in 25,000. Tyson, Shrader & Perlman (1938a) found phenobarbitone in 23 out of 37 samples of milk from 10 mothers who were receiving 2 grains daily, but there was no evidence of any effect on the babies. Mayo & Schlicke (1942) found pentothal in milk when they excised a branchial-cleft cyst from a woman 12 days post partum. Fourteen minutes after the injection of pentothal had ceased, milk from the right breast had a barbiturate concentration of 2.00 mg./100 ml.

Kwit & Hatcher also investigated the behaviour of morphine and codeine. After giving 16 mg. morphine subcutaneously, a trace of morphine, less than 0.1 mg., was found 4 hours later. Terwilliger & Hatcher (1939) described a woman morphine-addict, whose child showed apparent signs of addiction. But although the woman was receiving 128 mg. daily by injection, at no time did her milk show more than a trace of morphine. Kwit & Hatcher observed that codeine was not excreted in the milk at all, even after the oral administration of 32 mg. every 4 hours until 192 mg. had been given.

The same workers examined sodium bromide. A total of 15 g. was given to each of 2 patients in doses of 1 g. five times daily. 21 samples of milk were taken over 6 days. The first sample from one patient, and the first and second from the other did not yield bromide, but the other 18 samples did. Nearly 8 mg. were obtained from one sample, and most of the others yielded 2 mg. Thus mild bromism might result from babies drinking the milk of mothers taking sodium bromide. Van der Bogert (1921) reported a papulo-pustular eruption which developed in a child from this cause, and stated that "more than a trace" of bromide was discovered in the milk. Tyson, Shrader & Perlman (1938b) gave 10 women 6 g. sodium bromide daily for 3-5 days. Bromide was found in 37 out of 38 samples of milk, and there was clinical evidence of bromism in 4 of the babies, who were drowsy, and one had a rash.

4. Purgatives

Tyson, Shrader & Perlman (1937) have also examined the passage of purgatives into milk, recording the daily motions of mother and child, the purgative being given on the 5th day post partum. Aloin affected the bowels of 11 out of 33 babies, though evidence of aloin in the milk was obtained in only 7 out of 11 patients tested. Phenolphthalein affected the bowels in 10 out of 25 children, though there was no evidence of it in the milk. Kwit & Hatcher likewise found no phenolphthalein in breast-milk after giving 1.5 grains [100 mg.], and the finding of Tyson, Shrader & Perlman that the babies' stools were affected is surprising in view of the frequency with which phenolphthalein is given to nursing mothers. These authors found no senna or rhubarb in milk, and rhubarb had no effect on the babies. Calomel affected 2 out of 4 babies.

5. Other Substances

Unlike sodium bromide, iodide does not appear to enter the milk. Kwit & Hatcher found extremely small amounts of potassium iodide in samples of milk obtained after giving 3.8 g. on one occasion and 4.6 g. on another. Pommerenke & Hahn (1943) administered 65 mg. of radioactive sodium as the chloride, in orange juice, to four nursing mothers. Appreciable amounts of radio-sodium were recovered within 20 minutes of ingestion. In 2 hours (when the peak of excretion was reached) from 0.5-1.3 % of the amount fed/litre of milk had been recovered, the secretion subsequently diminishing.

Sodium salicylate and quinine are substances which are often taken over long periods, and might enter the mother's milk. Kwit & Hatcher gave 4 g., 2 g., 1.2 g. and 0.6 g. sodium salicylate to four patients in divided doses. Extracts of the milk collected 4 hours after the last dose contained from 1 mg. to 0.02 mg. sodium salicylate respectively, which are negligible amounts. Terwilliger & Hatcher gave 5 doses of 300 mg. each of quinine sulphate to two lactating women, and 7 doses of 640 mg. each to four women. Traces of quinine were found in the milk in every instance, in one case 30 minutes after ingestion. None was found 24 hours after administration. The amount recovered was once as high as 0.32 mg., but was generally of the order of 0.01 mg. or a trace.

6. The Milk of Animals

Observations have been made in two directions in animals. It is known that oestrogenic substances can be used to bring heifers into milk which have failed to become pregnant. Stilboestrol has been used in this way; tablets have been implanted under the skin and daily injections have also been used. It was naturally of importance to observe whether an oestrogen appeared in the milk itself. Lawson, Stroud & Williams (1944) showed that hexoestrol could actually be demonstrated in the milk of heifers, but they found that the amount was as little as 1 microgramme per pint (568 ml.) even when a tablet of 1 gramme was implanted.

The introduction of DDT as an insecticide to be sprayed on foliage has raised the question of whether cattle will suffer if they eat the foliage, or whether their milk will be toxic to those consuming it. Woodard, Ofner & Montgomery (1945), experimenting on the accumulation of DDT in the body-fat of dogs, found 0.06 and 0.04 mg. DDT per gramme of milk on two successive days in a bitch receiving 80 mg./kg./day of solid DDT. Telford & Guthrie (1945) gave food containing 0.1 % DDT to 3 rats with a day-old litter. Typical tremors occurred in the mothers and young and by the 18th day all except one mother and one nursling were dead. These two were placed on a normal diet and recovered. Nine adult rats fed on milk obtained from goats which were receiving 1 g. DDT/8-9 pounds [3.6-4 kg.] body-weight died with symptoms of DDT poisoning. Likewise, DDT poisoning exhibited by parturient rats fed on goats' milk from DDT-fed animals was passed on to the young of the rats. However, young goats suckling from DDT-fed mothers showed no ill-effects. But butter made from milk of DDT-fed goats and fed to rats produced DDT tremors. The authors concluded that intensive research was necessary on the toxicity of milk from cows ingesting DDT-sprayed foliage.

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MILK-BORNE DISEASE IN BRITAIN

A Brief Survey of the Position during Recent Years

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1 Bovine tuberculosis
2 Typhoid and paratyphoid fevers
3 Salmonella food-poisoning infections
4 Dysentery
5 Undulant fever
6 Streptococcal infections
7 Staphylococcal food-poisoning
References

Milk-borne diseases are still very much in evidence in Britain, and although undoubted progress has been made towards their elimination a great deal has yet to be accomplished to diminish their unnecessary prevalence. The subject arouses almost perennial controversy and discussion in the legislature, and in the medical and lay press, and will no doubt continue to do so until an entirely satisfactory method of control has been established. At the Annual Representative Meeting of the British Medical Association in 1945 this matter was again ventilated and attention was called to the urgent necessity for instituting measures of control. An editorial article which appeared in the *British Medical Journal* (1945) reviewed the position. It said that in 1943 the Government announced in a White Paper its intention of controlling the quality of the milk by making it impossible to sell milk in areas scheduled by the Minister of Food unless it was either heat-treated or obtained from disease-free dairy herds. Further, a Defence Regulation, issued in January 1945, specified certain milks which might be sold in specified areas but did not specify the area.

In April 1946, a debate on this subject took place in the House of Lords. One speaker put the yearly number of deaths from drinking tuberculous milk at 1,600 and the number of casualties at 7,000 to 8,000, to say nothing of other types of infection. The Government spokesman replied that the annual consumption of liquid milk in England and Wales was 1,075 million gallons[1] and of this 725 millions were heat-treated. Again, at the Annual Representative Meeting of the British Medical Association in July 1946, a resolution was adopted to the effect that the Council of the Association insisted that the Minister of Health and the Minister of Food should secure legislation immediately requiring all milk for human consumption to be pasteurized. Chalmers (1946) described how attempts have been made in Scotland to encourage the production of clean milk by increased premiums. In 1944 the premium for milk obtained from tuberculin-tested herds was increased to fourpence [£0.017] per gallon, and in 1945 arrangements were made whereby dairymen holding a licence under the Milk (Special Designation) Orders (Scotland) 1936-1944 to sell milk as " Pasteurized " or " Heat-treated " would receive a premium of one half-penny [£0.002] a gallon in respect of milk sold under one or other of these designations.

During the past few years several books have been published dealing with milk-production and milk-borne diseases. *The pasteurization of milk* by Wilson (1942) gives a very full account of the pros and cons of this vexed question. The book includes chapters on milk-borne infections, methods of rendering milk safe, and an account of the effects of pasteurization on the nutritive value of the milk, and it presents conclusive evidence on the need for the elimination of milk-borne disease. *This milk business* by Enock (1943), who is a mechanical engineer, deals largely with the various types of plant available for pasteurization, and advocates the " in-bottle " method, but one chapter is devoted to milk-borne diseases. *Pasteurisation* by Hill (1943) discusses the necessity for pasteurization and answers criticism of this method of making milk safe. The rest of the book is devoted to a discussion of the technical matters connected with pasteurizing plants and the methods of checking their efficiency.

1. Bovine Tuberculosis

Bovine tuberculosis is probably the most serious of all our milk-borne infections. There is an immense reservoir of possible sources of infection, and the means of eliminating

[1] [1 gallon = 4.54 l.—ED.]

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them by pasteurization are available only in urban areas. The report of the Committee on Tuberculosis in War-time of the Medical Research Council (1942) calls attention to the fact that at least 40% of cattle throughout Britain give a positive tuberculin-test, although the percentage of reactors varies in different areas, and that at least 6% of farm milk-supplies contain tubercle bacilli.

There has been a very definite increase in non-pulmonary tuberculosis, particularly in young adults, during the war, but there is little evidence to prove that the bovine type of tubercle bacillus has had an increased prevalence in these cases. Griffith & Munro (1944) summarized the literature on the bovine type of pulmonary infection. These investigations showed that in Scotland, out of a total of 2,769 cases examined, no less than 160 (or 5.7%) showed a bovine type of infection. In England, on the other hand, where 4,194 cases were typed, only 81 (or 1.9%) showed the bovine bacillus. Cutbill & Lynn (1944) tried to determine the mode of infection in 48 cases of bovine pulmonary tuberculosis, as shown in table I.

TABLE I. PROBABLE MODE OF INFECTION IN 48 CASES OF BOVINE PULMONARY TUBERCULOSIS

Mode of infection	Number of cases	%
Alimentary	16	33
Air-borne contact with cattle	10	21
Air-borne familial contact...	3	6
No evidence obtained ...	19	40
Total	48	100

Again, from the evidence collected by Griffith & Munro (1944) it would appear that in England and Wales about one-quarter of the cases of bovine pulmonary tuberculosis are infected through the intestinal tract and in Scotland about one-third of such cases.

As regards the incidence of the bovine type of bacillus in the various lesions of surgical tuberculosis, little fresh has been added to the exhaustive statistics produced by Griffith (1938). Two methods have, however, been suggested for the determination of the number of deaths due to the bovine type of bacillus. The first is that used by the Cattle Diseases Committee (1934) and this argues that, since the frequency with which the bovine type of bacillus is found in different clinical forms of tuberculosis is known, it is possible to estimate the deaths from the figures given in the Registrar-General's Annual Report. Wilson (1942) suggests the following alternative :—in the Adminstrative County of London where practically all milk is heat-treated, primary infection of bovine origin is no longer possible. All patients with non-pulmonary tuberculosis must, therefore, be infected with the human type of bacillus, and if in London a given number of cases of pulmonary tuberculosis are associated with a given number of cases of non-pulmonary disease, it is a simple matter to calculate how many non-pulmonary cases should be associated with pulmonary cases elsewhere in England and Wales. The difference between the calculated number of human infections and the total of recorded cases gives the number of bovine infections.

In an interesting paper, Lethem (1946) gives almost conclusive evidence of the value of pasteurization. The author points out that abdominal tuberculosis in young children is mainly due to the bovine type, whereas in most other non-pulmonary lesions the human variety occurs more frequently. Further, by 1939 the proportion of heat-treated milk had risen in London to 98%, whereas in other urban areas only 35% to 60% was pasteurized. The effect of this on the death-rate from abdominal tuberculosis is shown in table II.

TABLE II. ABDOMINAL TUBERCULOSIS: DEATH-RATE PER MILLION CHILDREN UNDER 5

[actual number of deaths in brackets]

Area	1921	1930	1938	1944
Administrative County of London	136(51)	24(8)	12(3)	6(1)
Combined County Boroughs	437(490)	157(166)	63(57)	35(32)
Combined Urban Districts	366(370)	134(370)	77(66)	42(14)
Combined Rural Districts...	252(176)	92(57)	63(61)	60(37)

The most significant fact is that in 1944 the death-rate for abdominal tuberculosis in London was only one-tenth of that in rural districts.

2. Typhoid and Paratyphoid Fevers

The investigational aspects of typhoid and paratyphoid fevers as milk-borne diseases have been very fully dealt with in a paper by Scott (1941). Again, further advances in phage-typing methods have been reported by Felix (1943) and by Felix & Callow (1943), and the development of phage-typing of both *Salm. typhosus* and *Salm. paratyphosus* B has been of great assistance in epidemiological investigations. Felix has stated that without this new laboratory-aid there can be little hope of determining the source of infection of many of the sporadic and small groups of cases that occur throughout the country. This is amply demonstrated in a paper by Bradley (1943) on the results of an investigation of an outbreak of 21 cases of typhoid fever which occurred during a period of 18 months and which were spread over different counties in the south of England. Eventually a small outbreak due to type D4 typhoid bacilli occurred on a farm where the farmer himself was found to be a carrier. It was then possible to associate the previous cases, which were also infected with type D4 bacilli, with this source, and to prove that this particular milk-supply was the vehicle of infection. At Kettering, paratyphoid epidemics had occurred in 1927 and 1936, while in 1940, 222 more cases were diagnosed and reported by Hogg & Knox (1941). The source of infection in this outbreak was cream-cakes from one bakery, where it was found that out of 32 male employees no less than 10 showed evidence of infection. The possibility of infecting milk through contaminated water used for washing utensils and dairy purposes generally has always to be kept in mind, and Parry (1942) has recorded such an outbreak in which *Salm. typhosus* was recovered

from the water. The epidemiology of paratyphoid fever has been studied extensively by Savage (1942). He believes that the incubation period in paratyphoid fever is fairly variable, that the disease may in some instances start with symptoms resembling a food-poisoning infection, and that the death-rate associated with it is very low. As regards spread, he believes that the transitory carrier is more important than the chronic one. During the past year also, two extensive outbreaks, one of typhoid at Aberystwyth, and the other of paratyphoid at Coatbridge, have been due to infected ice-cream. The Ministry of Health has prepared and issued a Draft Order (Ice-cream (Heat Treatment) Regulations, October 8, 1946), which will require the ice-cream mixture to be pasteurized before freezing. The possibility of setting up a bacteriological standard for the purity of ice-cream is also under consideration.

3. Salmonella Food-Poisoning Infections

Recent research on the antigenic structure of members of this group has added much to our knowledge, particularly in regard to their prevalence, their distribution in various countries, and the sources with which they are normally associated. In fact, the members of this group have become so numerous that for the identification of the more unusual types recourse must usually be made to the services of the Salmonella Typing Centre, which are available through the Central Public Health Laboratory in London. One paper by Bridges & Taylor (1944) gives details of various technical methods which can be employed for identification. Various workers have demonstrated that in calves and cattle the two most common Salmonellas are *Salm. dublin* and *Salm. typhimurium*, while *Salm. enteritidis* and *Salm. enteritidis var. rostock*, which are closely allied to *Salm. dublin*, are less frequent. Conybeare & Thornton (1938) published a report on a milk-borne *Salm. dublin* outbreak of gastro-enteritis in 100 individuals, and at the same time summarized the literature on this subject. Tulloch (1939) recorded two outbreaks of a similar nature which had occurred in Dundee some years previously. More recently, Sutherland & Berger (1944) described a further outbreak due to *Salm. dublin* in Yorkshire, involving 162 persons where the bulk-milk from the farm which was the source of supply contained *Salm. dublin*, but the milk from the individual cows did not. The faeces, however, from one cow were found to be positive.

4. Dysentery

During the early war-period there was a high prevalence of bacillary dysentery infections amongst the general population, but more recently there has been a considerable decline in its incidence. The most frequent type of infection was that due to *B. dysenteriae* Sonne, but infections with *B. dysenteriae* Flexner were also quite numerous. Faulds (1942, 1943) described two outbreaks of Sonne dysentery in Cumberland. One involved 43 out of a total of 72 customers supplied by a small farm, and the other involved 120 individuals who received their milk from a retail dairy. In the first instance, workers on the farm had had Sonne dysentery, and in the second, individuals at one farm which supplied part of the milk and two workers at the retail dairy were found to have the infection. Nisbet (1944) described another outbreak at Kilmarnock which involved 90 persons, and Rae & Smith (1945) reported a large outbreak of 252 cases. In this latter outbreak, 60 gallons of pasteurized milk were retailed at a dairy, where it was found that three members of the dairyman's family and one adolescent male worker had had symptoms of dysentery. Specimens of faeces from these individuals repeatedly showed *B. dysenteriae* Sonne.

5. Undulant Fever

The presence of brucella organisms in milk continues to be investigated. Thus, Duke (1940) recovered an organism from the milk of an accredited herd of 76 cows which gave all the cultural and serological characteristics of the melitensis variety. Further examination of the individual cows showed that 3 animals were excreting this organism. Again, Menton (1940) has examined 1,000 milk-samples from the Midlands of England, and of these 34.5 % showed whey agglutinations. When, however, these samples were inoculated into guinea-pigs, only 29.1 % showed the presence of *Br. abortus*, but on the other hand 9.1 % of samples which showed no agglutinins contained living *Br. abortus*. The sera of the guinea-pigs were examined at 3-, 6-, and 9-weekly periods after inoculation, and this method was found to give a higher percentage of positive results than if only one examination had been made at 6 weeks. Again, Jones (1943) examined bulk milk-samples obtained in the Liverpool and Kent areas, with the following results :—

Years	Number of samples	Number positive	% positive
1933–34 ...	314	48	15.2
1939–40 ...	408	59	14.2

There was some indication of a higher incidence of *Br. abortus* in January and a low incidence in August, but when samples were obtained from an individual cow or from small groups of cows this seasonal variation was not in evidence.

Despite the fact that a fair percentage of milk contains *Br. abortus*, the incidence of human infections is very low. Thus, the Annual Report of the Chief Medical Officer of the Ministry of Health for 1938 (1939) gave the total number of reported cases between 1926 and 1938 as only 474, but within the past few years several small outbreaks have been noted. Elkington, Wilson, Taylor & Fulton (1940) described an outbreak in which 26 out of a total of 400 boys at a boarding-school had a febrile illness, and of these 10 gave a positive agglutination-test. Cruickshank & Stevenson (1942) reported that in another boarding-school, 4 out of 54 girls between the ages of 7, 9 and 17 years, with a staff of 14 teachers and maids, had been infected from unpasteurized milk. Finally, in a third school at North Molton (*Monthly Bulletin of the Ministry of Health & Emergency Public Health Laboratory Service*, editorial, 1942), 4 girls between 9 and 16 years developed the disease.

6. Streptococcal Infections

There is little doubt now that when a milk-borne epidemic of scarlet fever or streptococcal sore throat does occur, the milk has been contaminated as the result of a streptococcal mastitis, the infection having been transmitted to the cow from human sources. These outbreaks are invariably due to Lancefield's Group A strains, which are infrequent pathogens in the cow, while on the other hand Lancefield's

Group B strains, which cause a widespread incidence of mastitis in milk-cows, are only rarely associated with human infections. Allison (1942) has summarized the reports in this latter type of infection. He has noted that 47 human infections were associated with pregnancy and 9 with endocarditis.

As regards Group A *Str. pyogenes* infections, Douglas, Smith, Sutherland & Watson (1942) recorded an outbreak which occurred at Elgin. Between 13 January and 2 March, 1939, in this town of 900 inhabitants, 214 cases of scarlet fever were notified, but many cases of sore throat also occurred. The peak day of the epidemic was 26 January, when 31 cases were reported. The common food-factor amongst the primary cases was the milk-supply from a registered herd of 100 cows, 68 of which were in milk. By examination of the milk it was shown that one cow was excreting large numbers of haemolytic streptococci from one quarter of the udder. The strain isolated from the cow, and 10 strains of haemloytic streptococci isolated from patients, all belonged to Lancefield Group A and Griffith's type 3. Dublin, Rogers, Perkin & Graves (1943) published a paper on streptococcal outbreaks in various countries in which the organsim had been typed serologically, and showed that type 3 was more frequently found than any of the others.

7. Staphylococcal Food-Poisoning

Few papers are published in Britain compared with the USA on outbreaks of staphylococcal food-poisoning. This is probably due to the fact that their occurrence in Britain is less frequent, but it is difficult to say to what this can be ascribed. The vehicle of infection in the USA is often cream-filled cakes, whereas in the occasional british outbreaks, cooked meats seem to be more often involved. Phage-typing of staphylococci as developed by Wilson & Atkinson (1945) has demonstrated 21 different types, and this has proved of value in epidemiological problems associated with food-poisoning. In fact this method of investigation would probably afford more satisfactory evidence of the connexion between the infected food and the illness of patients than determining whether or not a staphylococcus produces an enterotoxin. Macdonald (1944) has published an account of a small outbreak due to cheese made from goat's milk. Five individuals had supper shortly after 6 p.m. one evening, and between 10 and 11 p.m. four had diarrhoea, abdominal pain, and dizziness. Strains of staphylococci obtained from the faeces of one patient, from three samples of cheese, and from the milk of the goat, all appeared to be identical.

* * *

The problem of milk-borne disease could be solved so far as urban areas are concerned by the introduction of compulsory pasteurization. It is, however, admittedly more difficult to make this applicable to rural communities. A further need is the provision of a more complete veterinary service which would provide for a proper survey of diseases in cattle, and then proceed to tackle these in a systematic fashion. The present method in Britain of trying to stimulate the production of clean milk by awarding bonuses for various classes of milk is no doubt of benefit economically, but it does not provide the safeguard that the milk is free from human pathogens.

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BACTERIOLOGICAL CONTROL OF MILK

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A Methods of milk-testing
1 Plate-count test
2 Dye-reduction tests
3 Presumptive coliform-test
4 Keeping-quality tests
B Role of laboratory tests in milk-control
5 Control of milk distributed raw
6 Control of milk which is heat-treated before distribution
C Methods of assessing the sterility of milk-equipment
References

This discussion will be confined to those aspects of bacteriological control that are concerned with the cleanliness or keeping-quality of milk, and will not deal with the problem of safety or freedom from pathogenic bacteria. These two aspects of milk control are distinct and must not be confused.

Most of the bacteria which lead to poor keeping-quality are added to milk after it is withdrawn from the udder. Their numbers can be controlled by the adoption of clean methods at milking-time, by the use of clean sterile equipment in which to handle the milk, and by efficient cooling to prevent too-rapid proliferation.

Pathogenic bacteria of bovine origin, and occasionally from human sources (Bendixen & Minett, 1938), may be present in milk before it is withdrawn from the udder. Infection during subsequent handling from human cases or carriers of disease, contaminated water-supplies, or other extraneous sources, may also occur. Clearly therefore, precautions which may be adequate to ensure milk of satisfactory keeping-quality will not suffice to ensure its safety.

A. METHODS OF MILK-TESTING

There are numerous methods in use in different countries which are designed to give, by direct or indirect means, a measure of the cleanliness or keeping-quality of milk. No two milk-samples contain exactly the same number or types of bacteria and it is hardly to be expected that different methods of testing will give exactly the same answer. Moreover, no single test can give complete information about the bacteria in milk, and tests which are suitable for one particular purpose may be entirely inadequate for another.

Results by the same tests may be expected to vary widely unless standard techniques are rigidly observed. In this connexion, the need for some system of regular supervision of laboratories making official milk-analyses is emphasized by the results of a comprehensive survey of such laboratories in 40 States in the USA by Black (1943). None of the 281 laboratories surveyed followed implicitly the official methods prescribed (American Public Health Association, 1941). Realizing the importance of this factor, the Ministry of Agriculture and Fisheries has made provision (1944b) for the regular supervision of all laboratories engaged in making bacteriological tests of milk-samples under the National Milk Testing and Advisory Scheme.

The age of the milk and its temperature of storage have such a profound influence on the bacteria present, that the results of any test can have no possible meaning unless these factors are taken into account. When the temperature is favourable, bacteria in milk are in a constant state of change. Even in fresh milk, in which the bacteria are in the lag-phase and show no increase in numbers, respiratory and metabolic changes proceed, so that reduction-time measured by dye-tests, and keeping-quality may be expected to be shorter at the end than at the beginning of the lag-phase (Wilson, Twigg, Wright, Hendry, Cowell & Maier, 1935).

The figures in Table I for 23 samples of morning milk maintained at different temperatures from 11 a.m. on the day of production until 9 a.m. on the following morning emphasize the magnitude of the effect of temperature of storage on the bacterial count.

TABLE I. CHANGES IN THE COLONY-COUNT [30° C.] OF 23 SAMPLES OF RAW MILK STORED FOR 22 HOURS AT DIFFERENT TEMPERATURES

(Geometric mean count before storage : 32,360)

Storage temperature (°C.)	Geometric mean count (per ml.)
2—5	26,310
10	69,180
14	512,900
18	2,754,000
22	28,180,000

The effect of temperature varies markedly according to the type and number of bacteria gaining access to milk at the time of its production. Thus, milk which has been carefully produced and contains a small number of bacteria will deteriorate less rapidly than milk which has been less carefully produced (Table II).

TABLE II. THE EFFECT OF STORAGE FOR 22 HOURS AT DIFFERENT TEMPERATURES ON THE COLONY-COUNT, METHYLENE-BLUE RESULT, AND KEEPING-QUALITY OF TWO RAW-MILK SAMPLES OF DIFFERENT INITIAL BACTERIOLOGICAL QUALITY

Storage-temperature (°C.)	Sample A			Sample B		
	Colony-count (30°C.)	Methylene-blue test at 37°C. (hours)	Keeping-quality at 18°C. (hours)	Colony-count (30°C.)	Methylene-blue test at 37°C. (hours)	Keeping-quality at 18°C (hours)
2—5	1,900	11	46	41,000	7½	38
10	1,720	9½	44	48,000	7½	34
14	15,100	8	40	110,000	6½	26
18	500,000	6½	26	2,420,000	3	18
22	1,700,000	1½	22	16,600,000	1	6

Low atmospheric temperatures during winter, by restraining the multiplication of bacteria on the utensils between milkings as well as in the milk itself, render the task of supplying the consumer with milk of satisfactory keeping-quality relatively easy, whereas during hot weather in summer the keeping-quality of any but the most carefully produced milk may be unsatisfactory unless it is well cooled, or better still refrigerated.

Neglect, in interpreting the results of bacteriological tests, of the effect of temperature to which samples are exposed and the time of exposure has led to a great deal of misunderstanding. Clearly there can be no agreement between the results obtained in different laboratories without due regard to the overpowering effect of these two important factors (Mattick, McClemont & Irwin, 1935).

The choice of time and temperature of storage of samples before testing must largely depend on the object of the examination. If a measure is desired of the initial contamination of the milk, then samples should either be tested immediately or stored at a constant temperature until the test is begun. If on the other hand, as is more usual, a measure is required of the bacteriological quality of milk as delivered to the consumer or to a dairy for processing, the combined effect of the initial contamination and temperature of storage pending delivery must be taken into account, and samples should be taken at the time of delivery.

It must be emphasized, however, that tests made at the time that milk is delivered to the consumer may fail to indicate its subsequent behaviour. Thus, two milks which give identical results at the time of delivery may behave quite differently during subsequent storage, according to the temperature to which the milk has been exposed before delivery. Deterioration in the hands of the consumer may be gradual in milk which has been carefully produced but stored at atmospheric temperature until delivered, whereas milk which has been badly produced, but in which proliferation of bacteria has been suppressed by refrigeration before delivery, may deteriorate rapidly when stored at atmospheric temperature by the consumer.

A new approach to the problem of ensuring that test-results reflect the keeping-quality of milk in the hands of the consumer is apparent in the official tests which have recently been prescribed in Britain for heat-treated and pasteurized milk (Statutory Rules and Orders, 1944a ; 1944b ; 1946). Samples taken during delivery are stored at atmospheric temperature until between 9 and 10 a.m. on the following morning and then tested by the ½-hour methylene-blue test. Since milk is stored under conditions simulating those to be found in the average british household, that which satisfies the test can be expected to remain sweet until it is utilized.

Of the numerous tests which are in use for estimating the bacteriological quality of milk, consideration will be confined to those which are in general use in Britain.

1. Plate-Count Test

In the field of dairy bacteriology there is no other test which has been so widely used and so severely criticized as the plate-count. Until 1937 it was the official method for testing designated raw and pasteurized milk, but in that year it was replaced by a methylene-blue test for the examination of designated raw milk, and in 1946 by a modified form of methylene-blue test for the examination of pasteurized milk. In spite of its many shortcomings, the test is still widely used unofficially. For certain purposes, including the detection of thermoduric bacteria in raw and pasteurized milk, and for evaluating the sterility of milk-equipment, there is no satisfactory substitute.

If the plate-count is to be of any value, its limitations must be clearly understood. It does not give exact information as to the number of living bacteria in milk. Many of the bacteria occur in clumps, and those which develop into colonies are recorded as single organisms. Moreover, many of the bacteria in milk are fastidious in their growth-requirements and may fail to form colonies in the medium used for plating. Thus, addition of 1% sterile milk to the medium leads to increased counts with both raw (Hiscox, Hoy, Lomax & Mattick, 1932) and pasteurized milk (Anderson & Meanwell, 1933).

Counts are seriously affected by the temperature of incubation of plates. Even slight differences in incubation-temperature may affect the count (Pederson & Yale, 1934 ; Yale & Pederson, 1936). Maximum counts are usually obtained when plates are incubated at 30-32°C. (Yale, 1938 ; Hempler, 1940) and not at 37°C., but even at the lower temperature many bacteria in milk may fail to form colonies. Incubation at the lower temperature not only leads to higher counts, but for some purposes may be essential to ensure a true assessment of the bacterial flora. This is particularly the case with milk and milk-products that are, during processing, subjected to some form of heat-treatment (Abd-El-Malek, 1943 ; Hiscox, 1945).

Wilson (1935) favoured incubation of plates at 37°C., but so little information of a public-health value is afforded by the plate-count that this view can hardly be justified, bearing in mind the additional information that may be derived when plates are incubated at 30-32°C.

The main objection to the use of the plate-count for official control purposes is the very large error of estimation inherent in the method even when prescribed technique is closely observed (Malcolm, 1932 ; Mattick *et al.*, 1935 ; Wilson, 1935 ; Barkworth, Irwin & Mattick, 1941). Wilson (1935) estimated that the error of a single determination may be of the order of $\pm$ 90%, so that the true count of a sample with a recorded count of say, 100,000 per ml. may be expected to be somewhere between 10,000 and 190,000 per ml.

2. Dye-reduction Tests

Dye-reduction tests depend upon the ability of bacteria growing in milk to reduce the oxidation-reduction potential to a level at which the colour of the dye is either changed as with resazurin or completely discharged as with methylene blue. Dye tests therefore give a measure of the metabolic activity of the bacteria in milk, and in this way differ fundamentally from counting methods.

The reducing activity of different bacteria varies, but those which actively sour milk are in general active dye-reducers also (Wilson, 1935 ; Hobbs, 1939). Dye tests may, however, fail to indicate the presence of relatively inert bacteria which may be present in some milk-samples in large numbers. Thus Rowlands & Provan (1941) have shown that dye tests may fail to reveal the presence of thermoduric bacteria which may occur in large numbers in some samples of pasteurized milk, and Malcolm & Leitch (1936) found that during winter raw milk may contain large numbers of bacteria and still give a long reduction-time with methylene blue. It should be emphasized, however, that such types, because of their inert

characteristics, are unlikely to influence the keeping-quality of milk.

For routine control purposes, the dye tests possess certain advantages. They have a small experimental error, require a minimum of equipment, and can be done by relatively unskilled workers. They give as good a measure of the cleanliness or the keeping-quality of milk as any of the other bacteriological tests which are in general use.

Following the adoption of the methylene-blue test for the official examination of Accredited and Tuberculin Tested raw milk in 1937 (Memo. 139/Foods), several workers reported surprisingly good agreement between the placing of a series of samples of designated milk by this test and by the plate-count method previously used (Fairer, 1937; Orwin, 1938; Barkworth *et al.*, 1941).

For the routine examination of fortnightly samples from individual producers under the National Milk Testing and Advisory Scheme, the dye resazurin is used instead of methylene blue (Ministry of Agriculture and Fisheries, 1943). Fundamentally the resazurin and methylene-blue tests are the same. Resazurin, however, is reduced in two stages, from blue through various colour-tints to pink, and finally to white. The time taken to reach the pink stage is shorter than with methylene blue (Johns & Howson, 1940), and the time to reach the white stage slightly longer (Thomas, Thomas & Davies, 1939). A comparator is available to permit an accurate measure—in terms of disk numbers ranging from 6 to 0—of the change in colour of resazurin during reduction in milk (Davis & Thomas, 1940). By observing the disk value reached after a definite time of incubation at 37°C., a result can be obtained without waiting for complete reduction as with methylene blue.

In the routine resazurin test as used under the National Milk Testing and Advisory Scheme, an attempt has been made to compensate for the effect on milk-quality of day-to-day variations in atmospheric temperature. The time of incubation at 37°C. is varied according to the mean of the maximum and minimum temperatures at which the milk is held during the 24-hour period preceding testing. Thus, when the mean temperature[1] is greater than 60°F. the disk readings are recorded at the end of 15 minutes, and when less than 40°F. after 2 hours. This has not, however, succeeded in attaining the object of levelling the proportion of unsatisfactory samples at all seasons of the year. Thomas (1945) found that of 400,000 samples tested under the scheme, the proportion classed as unsatisfactory ranged from 2% when the mean temperature was less than 40°F. to 17% when it exceeded 60°F. and 25% when it exceeded 65°F.

The retention of the methylene-blue test for designated raw milk and the introduction of the resazurin test under the National Milk Testing and Advisory Scheme have led to some confusion in the minds of producers whose milk is tested by both methods. Comparison of the results by the two tests has, however, shown that there is in general good agreement, although individual samples may show wide differences (Egdell & Thomas, 1943; Thomas & Peregrine, 1944).

The time-factor in making a test to determine the suitability for acceptance of milk at the creamery-platform is highly important, and in this respect the 10-minute resazurin test possesses decided advantages for this purpose (Barkworth, Davis, Egdell, Rowlands & Watson, 1943; Thomas, Phillips & Andrews, 1943; Anderson & Wilson, 1945). In Britain this test is used as a basis of rejection of milk at all creameries with their own laboratories.

With the possible exception of their use for the detection of thermophiles, dye-reduction tests have not, until recently, found much support for the examination of pasteurized milk. Rowlands & Provan (1941) found that dye tests applied to samples of freshly pasteurized milk failed to differentiate between samples with widely differing bacteriological quality, but when samples were aged for 24 hours at 15.5°C. or 18°C. before testing, a better measure of keeping-quality was obtained. Based on these findings, they evolved a modification of the resazurin test to assist in the detection of contamination of pasteurized milk from plant-surfaces during its handling after heat-treatment (Provan & Rowlands, 1943a). Further work by the same authors (Provan & Rowlands, 1943b; Rowlands & Provan, 1944), which involved examination of samples of pasteurized bottled milk taken at fortnightly intervals during a period of 12 months from 27 dairies, showed that a ½-hour methylene-blue or resazurin test, applied to samples which had been stored before testing at 18°C. for 24 hours from the time of removal from the dairy cold-stores for delivery to consumers, provided a good indication of the actual keeping-quality of the milk, as well as a measure of the extent of plant-contamination and the care taken to ensure cool storage before delivery. Tests made on samples stored at atmospheric temperature instead of 18°C.—the procedure now adopted for official tests of heat-treated and pasteurized milk—while indicating keeping-quality in the hands of the consumer, failed to give an adequate measure of plant-contamination during winter, when atmospheric temperature was low. For plant-control purposes therefore, storage of samples at 18°C. or some similar temperature is necessary.

3. Presumptive Coliform-Test

Coliform organisms in themselves are not dangerous to human health, but in the examination of water they afford a delicate index of excretal pollution. The same significance must not be attached to their presence in milk, since they may be derived from dung, dust, or unsterile equipment-surfaces at the farm or at the processing dairy. Moreover they multiply rapidly in milk at temperatures of 50°F. or higher. In addition, the errors of estimation by the dilution-methods used are very large (Wilson, 1935). Clearly therefore, results of coliform-tests on milk must be interpreted with extreme caution, especially when tests are made on samples which have been aged at uncontrolled temperatures.

Coliform organisms are, however, undesirable in milk. They contribute to the rapid deterioration of keeping-quality (Barkworth, 1934), and lead to difficulties in the manufacture of dairy-products (Whitehead & Cox, 1932; Hiscox, 1934; Kelly, 1939; Crossley, 1942, 1946).

The coliform-test provides a good measure of the extent of contamination of pasteurized milk from plant-surfaces during cooling and bottling (Vernon & Walker, 1936; Crossley, 1946). A coliform standard has been adopted recently for pasteurized milk in Scotland (Statutory Rules and Orders, 1944c).

[1] [t°F. = 5/9(t-32)°C.—Ed.]

4. Keeping-Quality Tests

Keeping-quality may be defined as the time that milk will retain its original sweet flavour. It is the measure by which the consumer judges milk.

A measure of the true keeping-quality is afforded by holding samples at a constant temperature, usually 15.5°C. or 18°C., until the milk becomes tainted or clots when boiled (Ministry of Agriculture and Fisheries, 1934). The determination of the end-point by smell or taste is highly subjective, and an alternative procedure which gives an end-point closely in agreement with smell has been suggested by Anderson & Wilson (1945). This involves withdrawing portions at regular intervals and observing for the presence of clots when an equal volume of milk and 68 % ethyl alcohol are mixed.

Hiscox, Hoy, Lomax & Mattick (1932) found that the time taken to reduce methylene blue in raw milk stored at 15.5°C. agreed closely with the end-point by tasting: similar close agreement has been observed for pasteurized milk (Rowlands & Provan, 1944). This form of the methylene-blue test has been adopted for testing heat-treated milk in Scotland (Statutory Rules and Orders, 1944b).

While the other bacteriological tests that have been discussed afford an indirect measure of keeping-quality, the results are not highly correlated with the true keeping-quality: a value of r (correlation coefficient) ranging from about 0.6 to 0.8 has been recorded by different workers (Barkworth, Irwin & Mattick, 1941; Thomas, Bowie, Peregrine & Phillips, 1944; Anderson & Wilson, 1945). If, therefore, information concerning keeping-quality is what is required, the only absolute method is to measure keeping-quality, using one or other of the tests that have been mentioned.

B. ROLE OF LABORATORY TESTS IN MILK-CONTROL

To secure milk of satisfactory cleanliness and keeping-quality, laboratory tests are required to serve two different functions. They are required to assess the general level of quality of all milk-supplies, which involves frequent and regular testing of milk from all individual suppliers. They are also required to give information which will enable producers and processors to assess, and if necessary to correct, their methods, so as to ensure compliance with statutory standards.

Tests which are to be used for the first purpose should have a small experimental error and, since large numbers of samples are involved, should be simple and inexpensive. These attributes may not be as essential in tests used by the industry itself, or by those whose function it is to advise producers and dairymen rather than to administer statutory regulations. Moreover, tests which may serve for routine milk-grading may not be sufficiently sensitive to give information concerning the exact source of contamination of milk at the farm or at the dairy.

It must be recognized that routine testing will not in itself secure a milk of satisfactory keeping-quality. Testing alone is of little value unless measures are taken to advise producers and dairies experiencing difficulty in complying with prescribed standards and, in cases of persistent failure, to suspend the distribution of milk from such sources.

Upwards of 160,000 farms are engaged in producing approximately 1,300 million gallons[2] of milk annually in England and Wales at the present time. Except for a short period during early summer, when a small surplus may be available for manufacture, most of the milk is utilized for human consumption in liquid form. In these circumstances, selection of farms—so widely practised for instance in the USA—on the basis of ability to produce a superior-quality milk for liquid consumption is out of the question. Accordingly, a tremendous task is involved in securing an improvement in the bacteriological quality of all milk supplies, bearing in mind the poor facilities that are available on many farms on which we are obliged to depend even to maintain the present inadequate total output.

Milk reaches the consumer through various channels. Of a total liquid-milk consumption in England and Wales of 1,132 million gallons during 1945-6, 16 % was distributed raw by nearly 50,000 producer-retailers (*Home Farmer*, Facts and Figures, 1947). Some milk is distributed raw by dairies supplied direct from farms, or from larger dairies where it is brine-cooled. The remainder, consisting of much the greater part of the total, is supplied by dairies which pasteurize or heat-treat the milk before distribution.

The problems involved in controlling the keeping-quality of milk which is distributed raw, and that which is heat-treated before distribution, differ and will be discussed separately.

5. Control of Milk distributed Raw

So far no official bacteriological standard for raw milk other than that which is sold under the designations Tuberculin Tested or Accredited has been prescribed in Britain. The sooner this defect is remedied the better. A standard for keeping-quality has been prescribed for all heat-treated milk, and it seems reasonable also to demand a standard for milk which is distributed raw.

The testing of producer-retailer supplies by the routine resazurin test under the National Milk Testing and Advisory Scheme has done much to remedy the situation created by the lack of a statutory standard. For producer-retailer supplies, however, this test which is done on milk samples aged for 24 hours at atmospheric temperature may fail to give an assurance of adequate keeping-quality during summer. This applies particularly to milk produced at the evening milking which is delivered to the consumer on the morning following production, and is expected to keep sweet for at least a further 24 hours. In the test (Ministry of Agriculture and Fisheries, 1943), the period of incubation when mean temperatures exceed 60°F. is 15 minutes only, and milk which at 24 hours reduces resazurin in this time is unlikely to remain sweet until completely utilized by the consumer, usually 40-44 hours after its production.

6. Control of Milk which is Heat-treated before Distribution

Heat-treatment of milk is mainly confined to the larger dairies which receive milk from several farms. The first

[2] [1 gallon = 4.54 l.—Ed.]

task facing these dairies is elimination of milk which may be unsuitable for including in the bulk for processing, which involves careful scrutiny of every churn of milk received. A rapid test which could be applied to every churn of milk before it is tipped would be of the greatest advantage, but a satisfactory test for this purpose has not as yet been evolved.

The most rapid bacteriological test available is the 10-minute resazurin test (Ministry of Agriculture and Fisheries, 1942a), which is in operation under the National Milk Testing and Advisory Scheme at all dairies that have their own laboratory facilities. Even this test is too time-consuming to permit testing of every churn of milk. Consequently, dairies must rely largely on the ability of milk-receptionists to detect by appearance and smell milk which is unsatisfactory. Records of regular routine tests made of the milk of individual producers are of value in indicating supplies which are likely to be unsatisfactory.

Raw milk may contain large numbers of thermoduric bacteria which survive pasteurization. Most of these bacteria are inert in milk and will not be detected by any of the dye tests. Their detection involves laboratory pasteurization—145°F. for 35 minutes—of samples from each producer, and plating on milk-agar with incubation of plates, preferably at 30°C. instead of 37°C. (Anderson & Meanwell, 1933).

Fortunately these thermoduric bacteria are of no public-health significance (Hansen, 1932), and have little effect on the keeping-quality of pasteurized milk. Their presence in large numbers in raw milk is an indication of inadequate cleaning and sterilization of milking equipment, especially milking machines, on the farm. Thermophilic bacteria which proliferate rapidly at the temperature of "holder" pasteurization[3] may lead to trouble, especially when hot sections of milk-pasteurization plant are inadequately cleaned and sterilized. Thermophiles are less likely to lead to trouble when milk is pasteurized by the HTST process, as the temperature used—162°F.—is above the optimum for their growth (Hiscox, 1944).

The detection of thermophiles requires special methods: their presence is seldom revealed by plates incubated at 37°C. They may be detected by incubating methylene-blue tubes at 63°C. (Meanwell, 1939), by the Breed microscopical method (American Public Health Association, 1941), or by incubating milk-agar plates at 63°C.

The keeping-quality of pasteurized milk is largely determined by the bacteria which are added to the milk, after heating, from unsterile plant-surfaces during cooling and bottling. Provan & Rowlands (1943a) have shown that dye tests, applied to samples taken at various points during processing and stored for 24 hours at 18°C. before testing, afford a better indication of the source of contamination than the plate-count. Tests of such samples for the presence of coliform organisms are also valuable for this purpose, especially if samples are aged before testing (Vernon & Walker, 1936) and the results compared with those for samples from the same bulk of milk taken from the "holder".

C. METHODS OF ASSESSING THE STERILITY OF MILK-EQUIPMENT

Frequent reference has been made to the importance of unsterile equipment-surfaces as sources of bacteria in milk.

The problem of assessment of the cleanliness and sterility of milk-equipment may be approached from two different angles, according to whether a measure is desired of the probable effect of the residual flora on the bacteriological quality of the milk, or of the efficiency of the apparatus and methods. The former object can be achieved by suitable bacteriological tests on samples of the same bulk of milk taken at various stages in production or processing, and results obtained in this way are invaluable for tracing sources of contamination likely to affect the commercial life of the milk. A better assessment of the efficiency of the apparatus and methods used for cleaning and sterilization is possible by estimating the bacteria removed from equipment-surfaces by sterile rinses or by swabbing measured areas of surfaces which are not amenable to rinsing.

Only a proportion of the bacteria on surfaces is removed by rinse- or swab-methods, and careful standardization of procedures used is essential to secure reproducible results. Techniques for rinsing churns (Ministry of Agriculture and Fisheries, 1942b) and for swabbing equipment (Ministry of Agriculture and Fisheries, 1944a) have been issued and are in use extensively for the examination of churns and other equipment in connexion with advisory work under the National Milk Testing and Advisory Scheme. The application of these methods as a basis for advice has been instrumental in bringing about a remarkable improvement in the efficiency of churn-washing at dairies throughout England and Wales.

Special importance must be attached to the assessment of the sterility of milk-bottles. Empty bottles may be returned from houses where there is infectious illness, and their adequate sterilization before refilling at dairies is obviously of the greatest importance. There is considerable agitation in Britain, especially in public-health circles, for a statutory standard for the sterility of milk-bottles. The results of an exhaustive study by Mattick & Hoy (1937) and Hobbs & Wilson (1943) of the problems involved in washing bottles might well form the basis for such a standard. On a basis of the number of bacteria recovered from washed milk-bottles by a rinse-technique, Mattick & Hoy have suggested a standard of not more than 200 and Hobbs & Wilson not more than 600 bacteria per pint bottle [1 pint = 0.568 l.]. With adequate control of the strength and temperature of the detergent in bottle-washing machines, and precautions to avoid recontamination of bottles from subsequent clean-water rinses, there should be no difficulty in attaining either of these standards in practice.

[3] [See article by E. B. Anderson in this number (*BMB* 1118) for definitions of the "holder" and HTST processes.—ED.]

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EVOLUTION OF BACTERIOLOGICAL STANDARDS FOR MILK IN ENGLAND

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1 Selection of tests
2 Fixing of standards
3 Standards for ordinary milk
4 Standards for designated milk
5 Standardization of technique

The evolution of bacteriological standards in England can best be traced through the Acts and Orders and other control schemes which have been in operation since 1915, in which year measures for the control of milk assumed a modern outlook and were brought within the scope of a single set of regulations.

Before passing to those measures it is important to note that bacteriological quality is not a single quality, but must be judged from several viewpoints which differ in importance according to the treatment to which the milk is subjected before consumption, and the stage at which the milk is sampled.

1. Selection of Tests

If, for example, milk is sampled during delivery to the consumer, the important factors for which tests should be applied are safety and keeping-quality, and the tests and standards for these attributes may be quite different according to whether the milk is raw or pasteurized. Again, if a milk is sampled between the place of production and delivery to the dairy, standards to be set and the appropriate tests to apply would depend on whether that milk was to be pasteurized before consumption or sold to the customer without heat-treatment. If the former, the most appropriate test would be that for " pasteurizability ", and freedom from pathogenic organisms, although highly desirable, would be of lesser importance ; if the latter, safety and keeping-quality would be the essentials at whatever stage the milk was sampled.

Quite separate and distinct tests are required for the different attributes which combine to make up bacteriological quality, although alternative tests may be available to examine for the same attribute. The selection of tests must be made

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according to the facilities available for testing and after consideration of certain other factors. For example, if a milk-supply is to be tested for "safety", the results of a microscopical examination of the centrifuged deposit followed by inoculation into guinea-pigs will give a fairly complete answer concerning its freedom from pathogenic organisms of bovine origin, but if the milk is pasteurized a more satisfactory test would be the phosphatase-test for efficiency of pasteurization, an alternative which is not available for raw milk. Neither test would provide the complete answer, but either would provide enough information on which to base an opinion.* Again, if a sample of milk is to be tested for keeping-quality, a result can be obtained either by keeping the sample and testing at regular intervals until it becomes unpalatable, by testing for plate (colony) count, for methylene-blue reduction-time, for the resazurin-reduction figure, or by alcohol test. By standardizing the conditions under which the samples are taken and the tests are done, standards can be set which, when interpreted in the light of the treatment to which the bulk is normally subjected, will provide a basis for the control of any particular attribute of the milk-supply.

2. Fixing of Standards

Before setting such a standard, however, extensive experience is required of the behaviour of the bacterial populations in milk under different conditions of handling and treatment and their influence on the result of the test, and it is as a result of experience in the value of different tests that it has been possible to introduce standards and change them from time to time. Safety and keeping-quality are the two attributes contributing to bacteriological quality for which statutory standards have been set.

This is scarcely the place to enter into a discussion as to the comparative importance of safety or keeping-quality, or even of nutritive value, but a point which is frequently ignored is that, however nutritious a milk may be or whatever tests may have been applied to ensure its safety, the consumer will derive no benefit if the milk becomes unpalatable before it can be used. It is a matter for regret, therefore, that the importance of keeping-quality and cleanliness has at times been forgotten in stressing the importance of safety. The two qualities are supplementary, and to emphasize one to the detriment of the other is a mistaken policy. Safety, as applied to milk, means freedom from organisms capable of causing disease in man, and only one standard is possible. There is, therefore, no question of evolution of standards except in so far as different tests may be introduced, which bring about improved control. An indirect test for pasteurized milk which provides an unerring guide to the efficiency of pasteurization has recently been introduced as a statutory test. It is the phosphatase-test, and in so far as it provides information concerning pasteurizing efficiency, it goes a long way towards guaranteeing the safety of the milk, provided the milk has not been exposed to pathogenic contamination after heating.

The keeping-quality of milk, as the term implies, is the period which elapses between the time of production and the development of unpalatability. So long as the onset of unpalatability does not occur before the milk has been consumed or before the consumer has received the next delivery, the keeping-quality may be regarded as satisfactory.

3. Standards for Ordinary Milk

Milk & Dairies (Consolidation) Act 1915 Milk & Dairies (Amendment) Act 1922

Modern legislation for the control and improvement of the milk-supply was initiated by the Milk and Dairies (Consolidation) and (Amendment) Acts. These gave the President of the Local Government Board, later the Minister of Health, power to make orders which were intended to set out in detail the steps to be taken by the dairy industry and by the controlling authorities to ensure that the desired improvement would take place.

Milk & Dairies Order 1926

In pursuance of these powers the Milk and Dairies Order was made in 1926. This order aimed at improving the conditions under which milk was produced, handled and distributed, by setting minimum requirements for buildings used as cowsheds and dairies, by specifying the methods to be used for washing utensils and equipment, and generally laying down rules for the avoidance of contamination of milk at all stages between the cow and the consumer.

Neither of the Acts nor the Order mentions a bacteriological standard, and it is clear that there was no intention of setting such a standard. The obvious intention was to create conditions of handling which, if observed, would inevitably lead to improvement without the imposition of a bacteriological standard.

It is probable, however, that if in 1926 an attempt had been made to set a bacteriological standard with which all milk had to comply it would have been impossible to operate for several reasons. In the first place, milk-testing laboratories and staff did not exist in sufficient numbers; secondly, milk-testing methods were laborious and could not have been applied with the necessary frequency and in the numbers which would certainly be necessary to ensure adequate control; thirdly, most producers had not the necessary equipment or knowledge, and were incapable of complying with any bacteriological standard which could be regarded as reasonable. These reasons against the setting of a bacteriological standard no longer obtain today and, as will be shown later, a bacteriological (resazurin) standard for all milk has been in operation since June 1942. An account of the history of the development of the testing, advisory and educational services which led up to the present position would be too long to include within the scope of a single article, but it is sufficient to say that the provision of laboratories, the training of staffs and the application of suitable tests for control on a national scale, have been made possible by the Advisory Dairy Bacteriological Service of the Ministry of Agriculture, with the encouragement and co-operation of the National Institute for Research in Dairying. The education of producers has been achieved by means of clean-milk competitions and advisory schemes organized by the County Agricultural Education Staffs, and operated by them in conjunction with the Advisory Dairy Bacteriologists.

During this time the larger dairies were installing laboratories to an increasing extent and by means of bonus schemes were taking advantage of the county educational and advisory schemes. Unfortunately, selective buying on basis of tests tended to divert the better supplies into the larger dairies, and the poorer supplies were left to the smaller dairies without facilities for laboratory control. Some small dairies without these facilities imposed as one

condition of purchase that the producer must participate in a county clean-milk competition or advisory scheme. Many dairies paid the entry-fees, but the main point is that during the period between the wars all branches of the industry worked together in promoting improvement in the bacteriological quality of milk. By 1939 most producers, either directly or indirectly, had benefited from the educational and advisory facilities provided by national funds, and while it is true that no national bacteriological standard had been set for ordinary milk, experience had been obtained in the use of tests and in methods of milk-control, and the quality had improved to such an extent that the time was almost ripe for the setting of a national standard ; all that was required was the impluse.

On the outbreak of war in 1939, quantity became the keynote of production. Milk-producers became pre-occupied with the need for increased quantities of home-grown foods both for stock and for human consumption, and this, together with the shortage of labour, inevitably brought about a rapid deterioration in milk-quality. Milk was being lost through souring in increasing quantities, and this provided the impulse for the introduction of the National Milk Testing and Advisory Scheme by the Ministry of Agriculture and Fisheries in co-operation with the Ministries of Food and Health. The resazurin test was used, a uniform technique of testing was established, and national standards introduced for the first time with which all milk had to comply.

It must be stressed that this was an advisory scheme without statutory powers. It introduced three grades of milk called Category A, Category B, and Category C, which were equivalent to good, moderate, and poor keeping-qualities. Producers whose milk fell into Category C were advised and helped to improve it ; those who refused to improve were warned, given every chance, and finally, with the assistance of the Milk Marketing Board, were refused permission to supply milk for human consumption. The scheme has operated with the assistance and collaboration of all branches of the industry which is anxious that, whatever final form the wartime scheme may take, the national standards shall be retained.

4. Standards for Designated Milk

So far, the evolution of standards has been described only in regard to ordinary milk, but the powers granted to the Minister of Health by the Acts of 1915 and 1922 included the power to make orders for the introduction of designated milks and for controlling the conditions under which these special milks would be produced and sold.

Milk (Special Designations) Order 1922 Following the operation of schemes of an experimental nature, and in pursuance of the powers just mentioned, the Milk (Special Designations) Order was made in 1922 and introduced three grades of raw milk and one of heat-treated milk.

Ministry of Health Circular 356 ; 1922 Bacteriological standards were introduced which were believed to be

> " such as to provide milk that is superior to ordinary milk . . . and at the same time bring the production and distribution of the milk within the competence of all careful dairymen ".

Thus it was felt that standards could be set with which at least a limited number of producers and dairymen could comply.

TABLE I. MILK (SPECIAL DESIGNATIONS) ORDER 1922

Designation	Bacteriological standards		Other conditions
	Plate (colony) count (per ml.)	*B. coli* absent in	
Certified milk ...	30,000	0.1 ml.	(1) Produced from tubercle-free cows (2) Bottled at the place of production (3) Must not be treated by heat
Grade A (Tuberculin Tested) milk	200,000	0.01 ml.	(1) Produced from tubercle-free cows (2) Must not be treated by heat
Grade A milk ...	200,000	0.01 ml.	Produced from veterinary-supervised herds
Pasteurized milk (until 1/1/1924)	50,000	No standard	Heated to 145° F.—150° F. [63° C.—66° C.] for at least 30 minutes; cooled to 55° F. [13° C.]
(after 1/1/1924)	30,000	0.1 ml.	

These bacteriological standards were set for samples taken before delivery to the consumer, transported immediately to the laboratory and tested on arrival, and were thus intended to give the bacteriological condition of the milk at the time of sampling. It is clear that, since the place of sampling might be at any point between the farm and the consumer's door, the 24-hour period which might easily elapse between these points caused the standard to vary considerably according to the age of the milk at the point of sampling. The influence of time and temperature on the bacteriological condition of the milk was therefore not sufficiently appreciated, nor was the need for absolute uniformity in the methods of testing, as no detailed instructions were issued to serve as a guide in carrying out the test.

Milk Special Designations (Amendment) Order 1922 An Amendment Order was made in December 1922, introducing certain alterations which the brief period of operation of the original order had shown to be necessary. These mainly affected pasteurized milk and in this connection permitted the use until 1 July 1923, of " any process of pasteurization (including the flash process) capable of effecting the necessary reduction of bacteria".

No alteration was made in the bacteriological standard.

Milk (Special Designations) Order 1923 On 25 May 1923, a second Milk (Special Designations) Order was made which again altered the standards for pasteurized milk as from 1 July 1923, so that in the brief period of a year three Special Designations Orders were necessary, each introducing changes in one or other of the standards which experience had shown to be impracticable.

TABLE II. PASTEURIZED MILK

Order	Date	Bacteriological standards: Plate (colony) count (per ml.)	Bacteriological standards: *B. coli* absent in	Other conditions
Milk (Special Designations) Order 1922	before 1/1/24	50,000	No standard	Heated to 145°F.—150°F. for at least 30 minutes; cooled to 55°F.
	after 1/1/24	30,000	0.1 ml.	
Milk (Special Designations) Amendment Order 1922	before 1/7/23	unchanged	unchanged	Any process of pasteurization (including the flash process) capable of effecting the necessary reduction of bacteria
Milk (Special Designations) Order 1923	before 1/1/24	200,000	No standard	(1) After 1/7/23 heated to 145°F.–150°F. for at least 30minutes ;cooled to 55°F.
	after 1/1/24	100,000	No standard	
	Grade A milk (pasteurized)			(2) Must not be so heated more than once
	before 1/1/24	50,000	0.01 ml.	
	after 1/1/24	30,000	0.1 ml.	

5. Standardization of Technique

Memorandum 139/Foods 1929, Ministry of Health A notable advance was made in 1929 when the Ministry of Health imposed a standard technique for the sampling and testing of graded milk. Much work had been done in the interval, particularly by the Advisory Dairy Bacteriologists, which demonstrated the magnitude of the error likely to occur if the methods employed in the sampling and testing of milk varied, and the introduction of a standardized technique must therefore be regarded as a definite step in the evolution of bacteriological standards. Dairy bacteriologists had previously standardized their testing-techniques in 1924.

For a further period of 13 years no change in bacteriological standards took place, but during this time there was intensive research with a view to improving technique and investigating the value of the statutory and other tests for use in milk grading.

In 1935, the Medical Research Council[1] published a valuable and comprehensive survey of all the tests then known which were likely to be of value for milk-grading.

Milk (Special Designations) Order 1936 The result of this work appeared to show that a methylene-blue standard would overcome some of the disadvantages inherent in the combined plate-count and coliform standard for raw milk which had been current until that time, and in 1936 a third Special Designations Order was made which changed the nomenclature of the grades and introduced a methylene-blue standard for raw milk. The standards for pasteurized milk were this time left unchanged.

This order, which came into limited operation on 1 June 1936, and full operation on 1 January 1937, reduced the number of grade-designations, and in doing so made a single grade of Tuberculin Tested milk, thus eliminating the separate standard of 30,000 bacteria per cm.^{3} for milk bottled on the farm. Thus from June to December 1936, only one count-standard—200,000 per ml. with no coliform organisms in 0.01 ml. existed, and from 1 January 1937, the methylene-blue standard was introduced.

It is of considerable interest to note that in the new order permission was granted to pasteurize Tuberculin Tested milk while permission to pasteurize Accredited milk, the equivalent of the original Grade A milk, was withheld.

Memorandum 139/Foods January 1937, Ministry of Health The methylene-blue standards now set involved a period of ageing, equivalent to half a day, at atmospheric temperature before the test was begun, although the count-standards which still operated for the two types of pasteurized milk required the immediate transportation of the samples to the laboratory, or, if the period of transit was likely to be prolonged, immediate packing in ice until the test was begun.

It is of interest to note that a period of ageing at atmospheric temperature before testing was specified in 1924 for all samples tested by Advisory Dairy Bacteriologists in connexion with the Clean Milk Competitions and Advisory Schemes.

Circular 1533—1936 Ministry of Health Another point to note, which is not a change of standard but which implies a change of attitude towards a standard, is that the

TABLE III. MILK (SPECIAL DESIGNATIONS) ORDER 1936

Designations: 1923	Designations: 1936	Bacteriological standards: Methylene-blue reduction-time (hours)	Bacteriological standards: Coliform organisms absent in	Other conditions
Certified milk	Tuberculin Tested milk (Certified)	Winter 5½ Summer 4½	0.01 ml.	Produced from tubercle-free cows
Grade A Tuberculin Tested milk	Tuberculin Tested milk			
Grade A milk	Accredited milk			Produced from veterinary-supervised cows
		Plate(colony) count per ml.		
Grade A milk (pasteurized)	None	—	—	—
None	Tuberculin Tested milk (pasteurized)	30,000	No standard	Heated to 145°F.—150°F. for at least 30 minutes; cooled to 55°F. Must not be so heated more than once
Pasteurized milk	Pasteurized milk	100,000	No standard	

[1] Wilson, G. S., Twigg, R. S., Wright, R. C., Hendry, C. B., Cowell, M. P. & Maier, I. (1935) *Spec. Rep. Ser. med. Res. Coun., Lond.* No. 206

coliform test was required to be done only occasionally, although of many thousand samples tested in the writer's laboratory since 1936 none has been submitted for the methylene-blue test only.

For assisting in the control of pasteurized milk, this circular suggests that licensing authorities will find the phosphatase-test of value, but no standard was set with which the milk was required to comply for statutory purposes.

Milk (Special Designations) Regulations 1941 On 9 July 1941, regulations were made permitting the use of an alternative method of pasteurization which sanctioned milk which had been heated to not less than 162°F. [72.7°C.] for at least 15 seconds, provided that the apparatus was suitable and fitted with an automatic device to divert the flow of milk not adequately heated. No change in the bacteriological standards was made.

Milk (Special Designations) Regulations 1946 Finally, in 1946 the standards for pasteurized milk were again changed, the count-standard being finally discarded and a methylene-blue standard of ½-hour introduced together with a phosphatase-standard. The method of ageing and testing was carefully standardized, but unfortunately the specified method of ageing makes compliance with the conditions almost impossible during spells of hot summer weather. Early amendment of these conditions is essential.

Statutory Rules & Orders 1944 No. 65 Reference to standards for pasteurized milk would be incomplete without some mention of Heat Treated milk, which was introduced as a designation by the Ministry of Food in 1944. By a regulation, now generally referred to as " 55 G ", the type of milk sold in certain areas was restricted in such a way as to ensure that none could reach the public unless it complied with specific bacteriological standards. Tuberculin Tested milk and pasteurized milk could be sold without restriction provided that the conditions of the licences were observed. Accredited milk could be sold only if derived from, and therefore immediately traceable to, a single herd ; other milk could be sold only after heat-treatment by authorized dairymen in such a manner as would ensure its compliance with prescribed methylene-blue and phosphatase-tests.

This completes the account of the changes which have occurred up to the present time—changes which have involved the introduction of new tests and the alteration of standards as and when these appeared to be necessary or desirable. None of the standards has been high, but of recent years they have been such that compliance with them was possible for the average producer or dairyman without extravagant outlay on buildings, plant or labour.

TABLE IV. STATUTORY STANDARDS FOR DESIGNATED MILK

Methylene-blue reduction-time (hours)	Period & temperature of ageing	Designation
Winter 5½ Summer 4½	½-day at atmospheric temperature	Tuberculin Tested milk (certified) Tuberculin Tested milk Accredited milk
½	Until between 9 & 10 a.m. on the day after sampling at atmospheric temperature not exceeding 65° F.[18.3° C.]	Tuberculin Tested milk (pasteurized) Pasteurized milk Heat-treated milk

TABLE V. ADVISORY STANDARDS FOR RAW MILK

Resazurin disc-numbers	Period & temperature of ageing	Category
4 to 6	1 day at atmospheric shade-temperature	A
1 to 3½		B
0 and ½		C

For statutory purposes, the methylene-blue reduction-test is the basis of the bacteriological standards for designated milk both raw and heated. In addition, grades of raw milk must have no coliform organism in 0.01 ml., and heated milk must give a reading not greater than 2.3 Lovibond blue units for the phosphatase-test.

For routine advisory purposes, the resazurin test is used and has come to be generally accepted.

After some twenty years' experience of bacteriological testing of milk for both Statutory and Advisory purposes, of interpreting the results of tests and advising in cases of failure to comply with the standards, it is the writer's opinion that, whatever test is used and whatever standard is set, greater benefit is likely to accrue if standards are also set for buildings, equipment and methods. The maximum benefit is possible only if the three services concerned—bacteriological, advisory, and administrative—work closely in touch with each other.

* * *

CHEMICAL STANDARDS AND ANALYTICAL METHODS FOR MILK

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There is no legal definition of milk, and the word " quality " in respect of milk is used very loosely and sometime includes both chemical composition and bacteriological quality. These two properties are quite independent and unrelated one to the other.

The fact that milk contains fairly large proportions of fat, protein, sugar and salts has been known for a long time, but it was not until reasonably-accurate analytical methods, suitable for routine use, were devised, that any general knowledge was obtained of the way in which the chemical composition of milk varied. From a general point of view, the chemical constituents of milk are conveniently divided into two parts : fat, and the solids-not-fat. The fat includes also the lipoids, such as lecithin, and the fat-soluble vitamins A and D. The solids-not-fat fraction contains everything else—casein, albumin, globulin, lactose, mineral salts and the water-soluble vitamins B_1, B_2, and C.

For some time previous to about 1900, the commonly-used analytical methods for milk consisted of a total-solids determination by evaporation, and the measurement of specific gravity by a special hydrometer (usually referred to as a lactometer). The usefulness of the latter is derived from the fact that, whereas the fatty portion of milk has a specific gravity of about 0.9, the solids-not-fat have a specific gravity considerably in excess of 1.0. The specific gravity of milk is therefore lowered by increasing fat-content and raised by increasing solids-not-fat. By the use of suitable formulae it is possible, knowing the total solids (i.e. fat plus solids-not-fat), to estimate the fat and solids-not-fat separately from a knowledge of the specific gravity of the milk.

Introduction of Direct Fat-Estimation Methods

However, the gravimetric determination of total solids is not a suitable procedure for the routine examination of large numbers of samples, and it is also costly, since it requires a good balance. Various attempts were made to devise a simple routine method for the direct estimation of fat and, in the last decade of the 19th century, the Babcock and Gerber methods were introduced for this purpose. They consist essentially of treating the milk with strong acids which disrupt the protein membrane round the fat-globule and so allow the fat to form a continuous phase at the surface of the liquid, separation being accelerated and completed by centrifuging. The Babcock method is in almost universal use in North America, and the Gerber test is practically universal in Britain.

The development of these direct fat-estimating methods removed the necessity for the gravimetric method, and virtually the whole of the british milk supply is now controlled by the Gerber method, and the solids-not-fat tests are made by the lactometer method. The milk of some 165,000 british dairy-farmers is tested, usually once or twice a month, by these tests, and in addition bulk supplies are likewise tested.

Seasonal and other Natural Variations

The evolution of these simply analytical methods also resulted in giving the authorities fairly precise information about the composition of different sorts of milks at different times of the year and the effect of various factors on the composition of milk. This led to the ultimate adoption of chemical standards for milk. These were based upon the consideration of a large number of analyses made in all parts of the country at different times, and the presumptive standards adopted were 3.0 % for fat and 8.5 % for solids-not-fat.

TABLE I. EFFECT OF BREED OF COW ON MILK SOLIDS

Breed	Fat (%)	Solids-not-fat (%)	Protein (%)	Lactose (%)	Ash (%)
Jersey ...	5.14	9.59	3.80	5.04	0.75
Guernsey ...	4.98	9.57	3.84	4.98	0.75
Ayrshire ...	3.85	9.05	3.34	5.02	0.69
Shorthorn ...	3.63	8.94	3.32	4.89	0.73
Friesian ...	3.45	8.48	3.15	4.65	0.68

The fat is by far the more variable factor, being easily influenced by such factors as breed of cow, yield, the time of the year, stage of lactation, etc. The content of solids-not-fat is much more constant and, although influenced to some extent by the same factors that control fat, varies between much narrower limits. For this reason it was possible to make for the solids-not-fat a chemical standard much closer to the average value than in the case of the fat. The latter varies from about 3.4 % or lower in May, when the yield of milk is at its highest and the fat-content at its lowest, up to about 3.9 % or even higher in December. The standard of 3.0 % was adopted on the argument that no milk produced from an ordinary herd in Britain would under normal conditions ever fall below 3.0 % in fat-content. Similarly the value for solids-not-fat normally varies from about 8.6 % to 8.9 %.

TABLE II. FACTORS AFFECTING FAT-CONTENT

Increase	Decrease
Good management	Feeding cod-liver oil
Short milking-interval	Long milking-interval
Complete milking-out	Incomplete milking-out
Young cows	Old cows
Later stage of lactation	Flush of milk (2nd to 5th months)
Cold weather	Warm weather
Moderate exercise	Rest
	Abnormal conditions, excitement, etc.
	Inexpert milkers

(Other factors are the individuality of the cow and breed.)

TABLE III. FACTORS AFFECTING CONTENT OF SOLIDS-NOT-FAT

Increase	Decrease
Young cows	Mastitis (disease of udder)
	Old cows
Later stage of lactation	Flush of milk (2nd to 5th month)
	Indoor feeding
Spring pasture	

(Broadly speaking, the fat-content of milk is more variable than the content of solids-not-fat, which is fairly constant.)

The effect of various factors on the fat and solids-not-fat content of milk is illustrated in tables I, II, III and IV. Different sets of figures give slightly different results for breed-values, but all show quite clearly that Jersey and Guernsey milks are the richest and Friesian is the poorest. There has been a slight fall in the average solids-not-fat content of Britain's milk over the past 20 or 30 years. Although the exact reasons are not known, it is probable that the increase in the number of Friesian cattle has been a major factor.

TABLE IV. SUMMARY OF ACCURATE (REFERENCE) AND SIMPLE ROUTINE TESTS FOR MILK

Constituent	Accurate tests	Routine tests
Fat	Röse-Gottlieb ... Adams ... ... (ether-extraction)	Gerber Babcock (acid-centrifugal separation)
Solids-not-fat ...	Gravimetric ... ... (evaporation of moisture & correction for fat)	Lactometer (specific gravity & correction for fat)
Added water ...	Freezing-point ...	Lactometer & conductivity-measurements
Lactose ...	Polarimetric	Polarimetric
Protein (total)	Total nitrogen (Kjeldahl)	Sørensen titration (with formalin)
Casein ...	Precipitation at pH 4.6 & weighing	Precipitation at pH 4.6, redissolving & Sørensen titration
Salt (NaCl) ...	Silver titration after digestion with HNO_3	Conductivity
Ash	Heating to dull-red heat	—
Visible dirt ...	Official Society of Public Analysts method (centrifugal)	Filter-pad or "sediment tester"

(Normally only fat and solids-not-fat tests are made on milks.)

Detection of Adulteration with Water

In early years, there was little control of the quality of milk, and the sale of milk was in the hands of a large number of small vendors, some of whom were not too scrupulous, and the proportion of adulterated milk was undoubtedly high. There was available no specific test to detect the addition of water to milk, and the authorities therefore had to adopt the basis that if milk fell below the presumptive standards of 3.0 % fat or 8.5 % solids-not-fat it should be presumed to be watered unless the contrary was shown. This worked very well in practice, since the milk-seller could always resort to the "appeal to the cow" test. This meant that, if accused of watering his milk because of its low content of solids, he could "appeal to the cow", or have samples taken from the milk as produced from his herd. If the tests on milk as taken agreed with those of his milk as sold to the public, than it was obvious that his milk was genuinely deficient in fat or solids-not-fat, and had not been adulterated.

Differentiation of Adulterated and Pathological Milk

In the course of time it became recognized that the solids-not-fat could have a low value from a pathological cause not previously suspected—mastitis. This disease is an inflammation of the udder caused by certain streptococci and other organisms which often results in the secretion of milk low in solids-not-fat. Such milk, usually called "abnormal milk" or "mastitis milk", often has a solids-not-fat content of less than 8.5 %, and until scientific knowledge extended and a more accurate test for added water became available, such milk was often suspected.

The solution to this problem came when the development of the freezing-point test gave public analysts a method for the more certain detection of added water in milk. This test depends upon the fact that genuine milk has a freezing-point which usually lies between −0.540 and −0.550° C. In a small proportion of samples from individual cows the freezing-point may be as low as −0.560° or sometimes as high as −0.530° C.

Following upon this discovery there has been a general agreement amongst dairy-chemists and public analysts that if milk has a freezing-point higher than −0.530° C., then it can certainly be assumed that the milk contains added water. The adoption of this as the standard gives a tolerance-equivalent to about 3 % water, since the average freezing-point depression is about 0.544° C. It is, therefore, customary nowadays for milks to be tested first by the fat and solids-not-fat test and then, if either is suspiciously low, for a freezing-point test to be made. The freezing-point test is not yet a statutory test, but it is now often accepted in a court of law as supporting evidence for or against the allegation that the watering of milk has taken place.

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MODERN METHODS OF HANDLING AND DISTRIBUTING MILK

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1 Production
2 The collecting creamery
3 Transport
4 Processing or pasteurization
5 Bottling
6 Care in the home
References

Modern methods of handling this important food are concerned with the object of delivering to the consumer a physically-clean, bacteriologically-safe product with the nutritive value impaired, if at all, to the minimum extent possible.

1. Production

As the conditions of production on the farm have an important effect on the efficiency of the subsequent handling, the review of events must start here. The principles governing the production of a clean safe milk are simple and have long been known, but it is only in comparatively recent times that their importance has been fully appreciated.

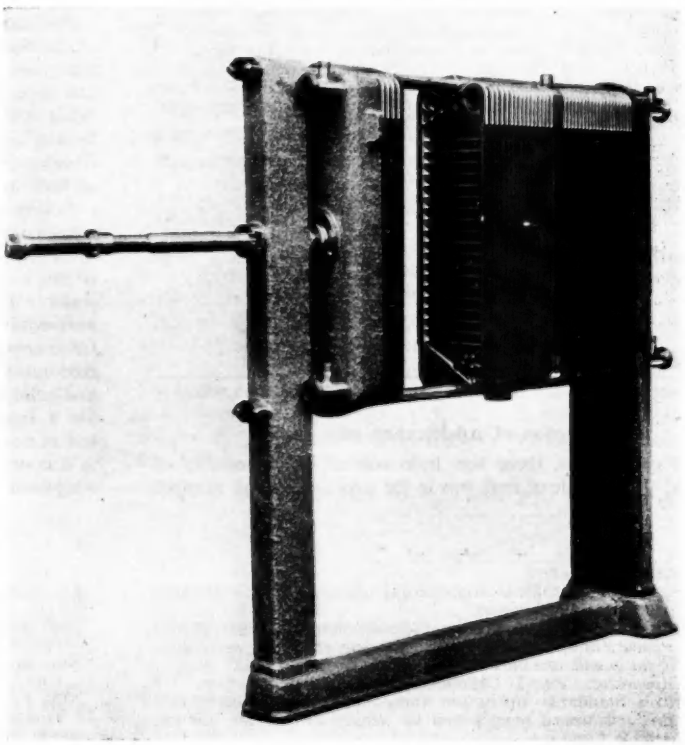
In properly-managed herds the cows, the only animals of importance for the production of milk in Britain, are free from disease, *i.e.*, *M. tuberculosis* and *Br. abortus*, and clean, *i.e.*, free from extraneous dirt, particularly on the teats, udder and flanks. The milker and those associated with the dairy, besides being clean in person, are free from communicable diseases such as septic sore-throat, or organisms of the typhoid and paratyphoid group. The utensils used are cleaned and then sterilized by treatment with steam or boiling water. This proviso applies particularly to the most modern types, such as the small top-pail and the milking-machine, both of which are advantageous if correctly cleaned and sterilized, but if not the results may be worse than those obtained by the old method of hand-milking. Although milk produced under the satisfactory conditions outlined above will keep for considerable periods without cooling or refrigeration, this is necessary if there is delay in utilization, particularly when the atmospheric temperature is high.[1] Although much milk is still cooled by standing the cans in cold water, it is now more customary to pass the milk over a corrugated-surface refrigerator which may be cooled by water or, in the more advanced types, by means of a direct-expansion refrigeration-unit. Whatever the method, it is usual to cool to at least 60°F., lower if possible.[2] The milk is poured into cans, generally nowadays of 10-gallons capacity[3], provided with mushroom-shaped lids which prevent the access of any foreign matter, whether liquid or solid. These are a great advance on the old type with drop-in lids.

It is now the practice for the creamery to provide the cans, which have been washed with hot water, scalded with steam, and dried with hot air in mechanical washers capable of handling up to 300 cans per hour. Rapid transport of the cans between creamery and farm and vice-versa is accomplished by motor lorry, thus widening the area from which supplies may be collected.

In this section, the main advance has been the greater appreciation and application of hygienic methods in production, and on the mechanical side the introduction of the mechanical instead of the manual washing of the cans.

[1] [See article by A. Rowlands in this number (*BMB* 1115.—ED.]
[2] [t°F. = 5/9(t-32)°C.—ED.]
[3] [1 gallon = 4.54 l.—ED.]

FIG. 1. PLATE-TYPE COOLER



The milk is pumped through the cooler, where it is cooled first by water and then by refrigerated brine to a temperature of 38–40°F. [3.3–4.4°C.]

2. The Collecting Creamery

Although creameries have long existed in milk-producing areas, their function has changed ; at one time concerned mainly with limited local sales and the manufacture of cream, butter and cheese, they have now become specialized links in the chain of distribution to the urban communities which, before their increase in size, received the milk direct from the producer by rail transport in cans usually of 17-gallons capacity, in which period considerable losses occurred through souring in unfavourable weather. Nowadays, on receipt at the local creamery, each can of milk is examined by inspectors who have been trained to detect by odour any milk which exhibits signs of deterioration or other abnormality. Such milk, together with that of other producers who may be suspected of not providing the grade required, is subjected to a dye-reduction test in the control laboratory which for this purpose operates the National Milk Testing and Advisory Scheme of the Ministry of Agriculture. This test is a rough indication of the numbers and activity of the organisms in the milk, and thus provides an objective test of its suitability for consumption. Milk which does not pass is returned to the producer. Consignments which are of a satisfactory nature are tipped into a tank of about 50-gallons capacity, the weight of the milk in which is indicated on a dial. From here it is pumped through a plate-type cooler (fig. 1), in which it is cooled first by water and then by refrigerated brine to a temperature of 38-40°F. All plant through which milk is passed is previously thoroughly cleaned, followed by sterilization with steam or hot water at about 180°F.

FIG. 2. INSULATED MILK-TANK FOR TRANSPORT BY ROAD

The milk passes directly from the cooler into the tank, which is of glass-enamelled or stainless steel and of 1,000–3,000-gallons capacity. The insulation is usually of cork or rubber

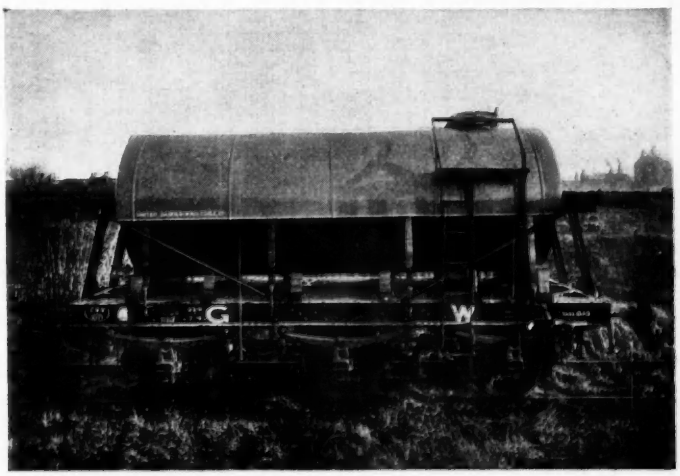
3. Transport

From the cooler, the milk passes directly to insulated tanks of glass-enamelled or stainless steel of 1,000–3,000-gallons capacity, mounted on chassis suitable for road or rail transport (fig. 2, 3). The insulation is usually of cork or an expanded-rubber product protected by an outer metal sheath. A man-hole is provided for access, and a suitable air-vent and cock for withdrawal of the contents. The fittings are reduced to a minimum to allow of easy cleaning, which is accompliished by rinsing with cold water, washing with a detergent delivered in the most modern method by a high-pressure jet ; finally sterilization is effected by blowing in live steam for about 15 minutes. Sometimes, for the last stage, a solution of sodium hypochlorite containing 200 parts per million of available chlorine is used, but steam is to be preferred. In such tanks, the contents can be transported considerable distances in hot weather with only a small rise in temperature. This refrigeration at the creameries and transport in bulk is the major revolution which has taken place since the 1914-18 war.

Milk is a biological fluid of high nutritive value for bacteria, whether harmful or harmless, and therefore, in order to avoid the transmission of pathogenic organisms, and to increase the keeping-quality, in all enlightened british cities and towns the raw product is now subjected to some form of heat-treatment, usually that known officially as pasteurization. This secures the freedom from pathogenic organisms which is of vital importance to the health of dense communities, and avoids economic loss from souring, particularly where household refrigerator-storage is not available, a common fault in Britain.

On arrival at the processing-depot, the milk is discharged from the transport-tanks, either by gravity or compressed air, into intermediate-storage tanks of glass-enamelled steel, stainless steel, or aluminium. If there is likely to be a delay in subjecting the milk to the heat-treatment, the temperature is again reduced to 40°F. by passage through a plate-cooler as, at this temperature or below, there is no multiplication of those bacteria which cause deterioration.

FIG. 3. INSULATED MILK-TANK FOR TRANSPORT BY RAIL



4. Processing or Pasteurization

There are two methods of pasteurization officially recognized—the " holder " and the High-Temperature : Short-Time (HTST). The regulation covering the former is that " the milk shall be held at a temperature of not less than 145°F. and not more than 150°F. for at least ½ hr.", and the latter that " the milk shall be retained at a temperature of not less than 162°F. for at least 15 seconds".

These conditions are based on the minimum time required to destroy the most resistant pathogenic organism, viz. *M. tuberculosis*, with an ample margin of safety.

On its way to either type of pasteurizing plant, the milk is pumped either cold or warm through centrifugal cleaners or cloth filters to remove any extraneous matter which may have gained access either at the farm or subsequently. It is then raised to the required temperature by passage through a plate-type regenerative heater in which the hot milk coming from the plant serves to heat the incoming milk, itself being cooled in the process. The final heating to the required temperature is accomplished by means of circulating hot water in a similar plate-type heater.

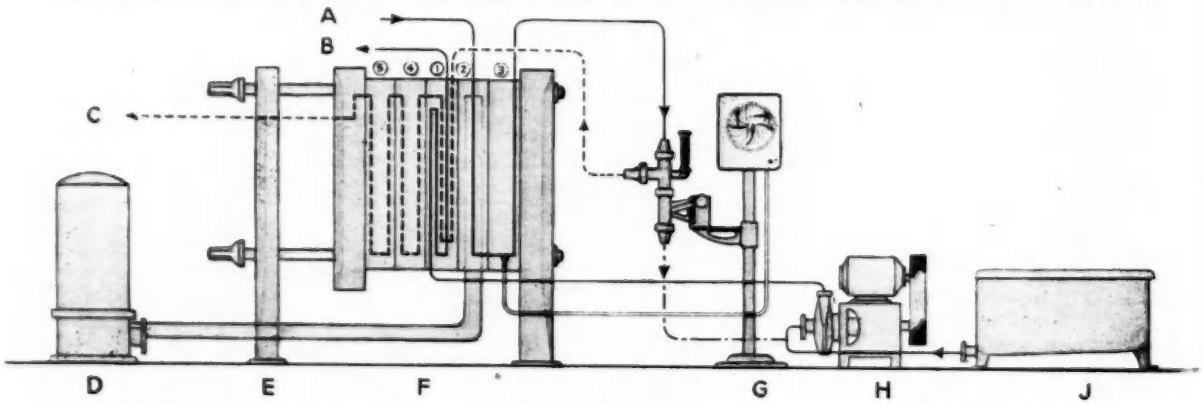
In the " holder " or " batch " process, the milk thus raised to 145°F. passes to the holding-vessels, which may have a capacity of from 100–1,000 gallons. The holding-time is automatically controlled in such a way that the discharge-valve is opened after the required period has elapsed. Recorders registering the temperature and time of holding are fitted to all such plants.

The HTST process requires more complicated plant and more delicate control, but has the advantages that it takes up much less space and is continuous in operation. Plants capable of processing 2,000 gallons per hour are now in existence. The raw milk is pumped to the regenerative heater through a constant-flow device. This is an essential part of the plant because, with the very short holding-time of 15 seconds, any variation in flow would involve considerable inaccuracy. The milk then passes to the holding-section, which is an enlarged plate, placed at the end of the heating-section of the plate-heater, and of such capacity that the milk passes through it in not less than 15 seconds. The exit-pipe from this holding-section is fitted with a flow-diversion valve actuated by a solenoid or by compressed air, either of which is brought into operation by a system depending on a mercury or vapour-in-steel thermometer fitted into the exit-pipe. The effect of this device is to cause the milk to be diverted back to the raw-milk tank if its temperature falls below that set for operation. At the same time a warning-bell or light signals the position to the operator. When the correct temperature is regained, the diversion-valve is re-set either automatically or by hand. With this mechanism it is impossible for any underheated milk to pass forward. Recently, thermo-electric couples have been suggested instead of the thermometers referred to, the claim made being that the unavoidable lag between the fall in temperature of the milk and the operation of the control-mechanism is much reduced, thereby allowing the process to be conducted much nearer the permissible minimum temperature of 162°F., with less reduction in the volume of cream forming on the cold milk. This system, however, is still in its infancy, and it is at present the usual practice to operate at a temperature 1°F. above the legal minimum and for about half a second longer.

The usual recording-instruments are provided to give on the chart a permanent record of the temperature during operation.

By whatever process the milk is pasteurized, it is immediately cooled to 40°F. by means of the incoming cold milk referred to above, followed by cold water and finally refrigerator-brine. It is quite usual for the whole of the heating and cooling systems to be combined in one unit. Fig. 4 is the flow-diagram of such a complete unit of an HTST plant including the holder. Fig. 5 is an illustration of the plant itself. On the left is the combined heating, pasteurizing and cooling unit, in which is also incorporated the filter. On the right is seen the cabinet housing the controlling and recording instruments, and just to the left of this the flow-diversion valve. Fig. 6 shows the construction of the plates, between pairs of which the milk passes with the heating or cooling medium on each side.

FIG. 4. FLOW-DIAGRAM OF A COMBINED HEATING AND COOLING UNIT OF AN HTST PLANT



A From filter
B To filter
C Finished milk
D Hot-water-circulating set
E Filter
F Heat-exchanger
1 Regenerator
2 Heater
3 Holder
4 Water-cooler
5 Brine-cooler
G Control-panel and flow-diversion valve
H Raw-milk pump
J Receiving-tank

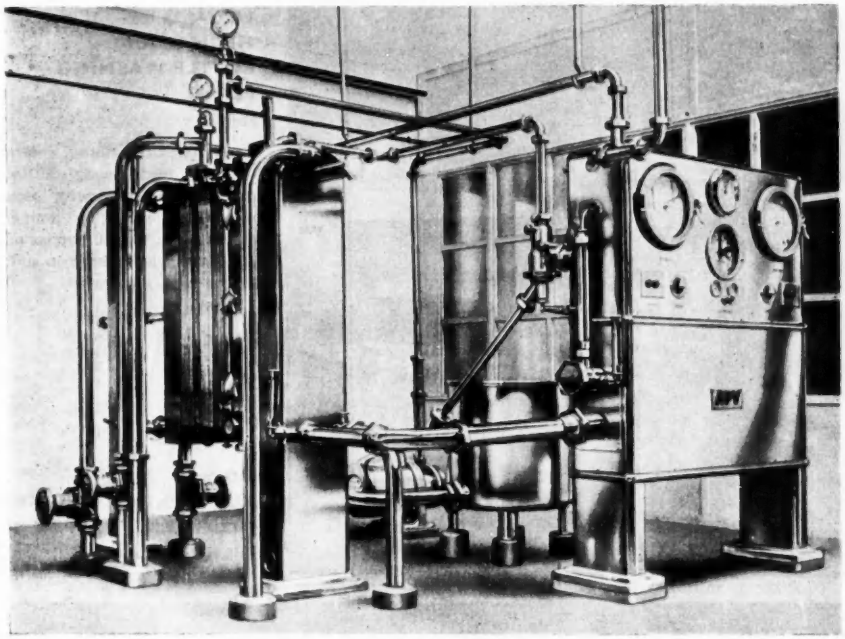
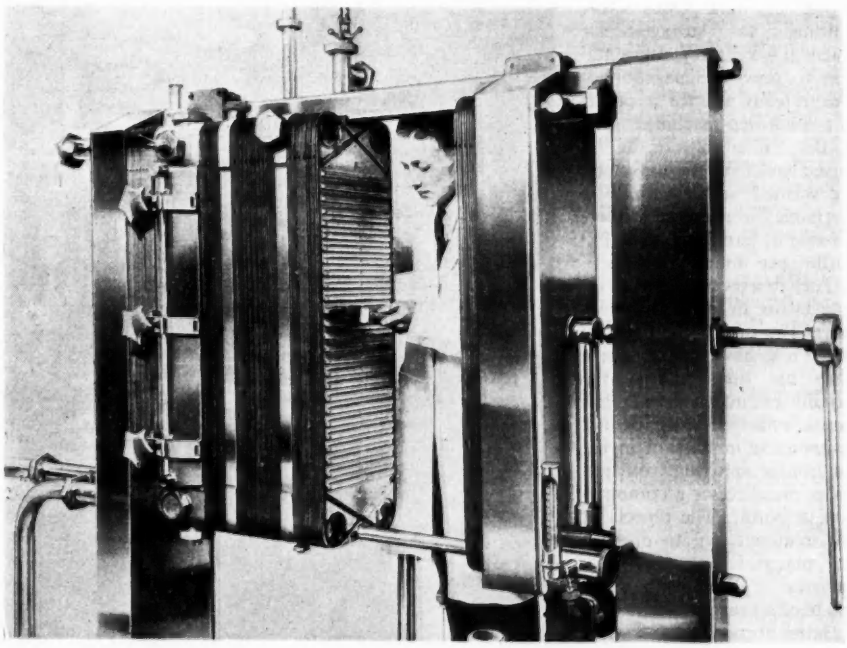


FIG. 5.
HTST HEAT-TREATMENT PLANT EMBODYING A COMBINED HEATING AND COOLING UNIT (left)

A flow-diagram of this plant is shown in fig. 4.
For further description, see text

FIG. 6.
PLATES OF THE HEATING AND COOLING UNIT OF AN HTST PLANT

The milk passes between pairs of the plates, with the heating or cooling medium on each side



Accurate as are the controls and recording instruments on modern plants, there was until recent years no satisfactory test which could be applied to the milk itself to confirm that the processing had been satisfactorily achieved. This most desirable goal was achieved when Kay & Graham (1935) published what is known as the phosphatase test in a form suitable for plant-control. This test depends on the fact that milk contains an enzyme, a phosphomonoesterase capable of hydrolyzing organic phosphates under certain defined conditions. By great good fortune this enzyme is destroyed under the time-temperature combination used for pasteurization. Briefly, the milk is incubated with a buffered solution of disodium phenyl-phosphate, and if the enzyme is absent no phenol is set free by hydrolysis. But if, because of under-treatment or contamination with raw milk, enzyme is present, phenol is set free and its quantity is estimated colorimetrically by a suitable reagent. The test is so sensitive that the presence of 0·25% raw milk, or a deficit of 1·5°F. below the required minimum temperature of 145°F. in the holder process, can be detected. Out of the thousands of tests made, in no instance has the presence of *M. tuberculosis* been detected by animal inoculation in milk which has passed the test.

Mention should be made of the in-bottle process, in which the whole operation of heating and cooling is carried out in the bottle, but there is insufficient independent evidence on which to base a considered judgement.

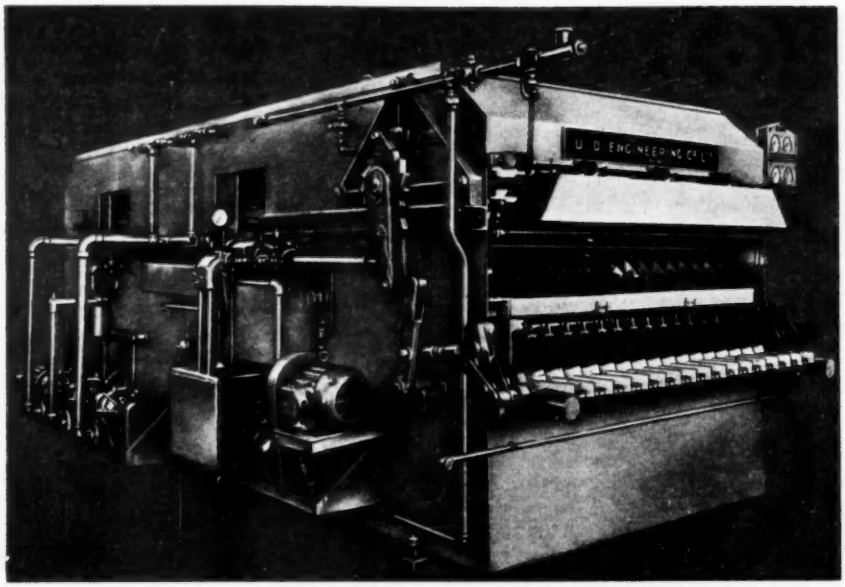
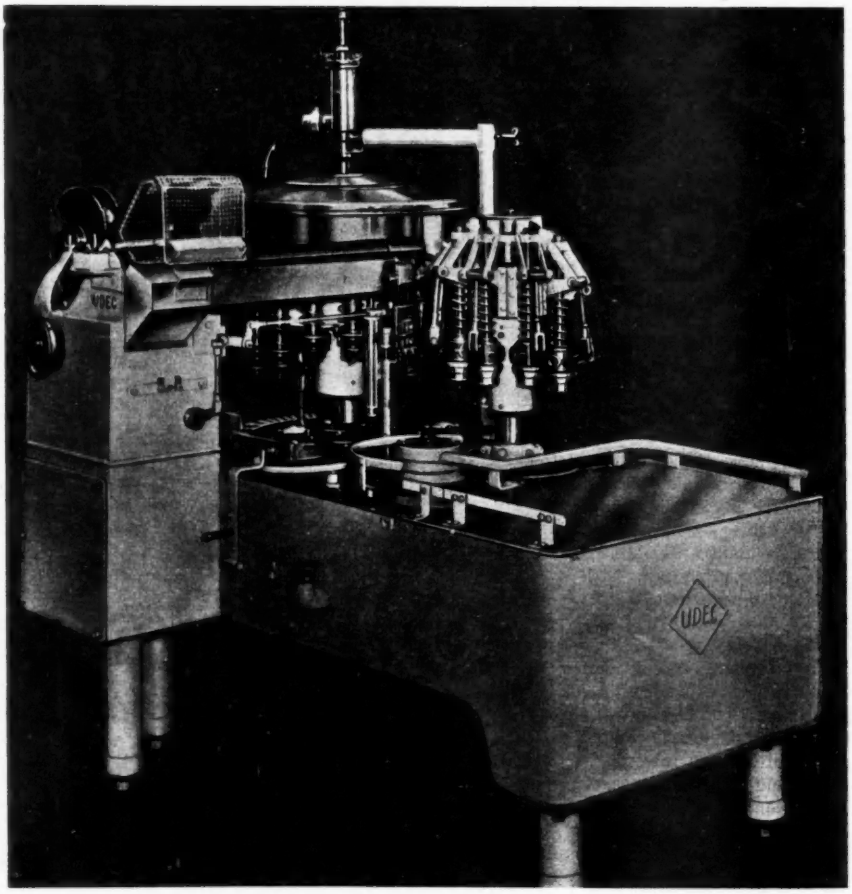


FIG. 7.
MECHANICAL BOTTLE-WASHING PLANT
(left)

The bottles are rinsed, treated with hot caustic-soda solution, and rinsed again with clean water at descending temperatures. Up to 160 bottles per minute can be treated in units of the type illustrated

FIG. 8.
AUTOMATIC COMBINED FILLER AND CAPPER OF MILK-BOTTLES

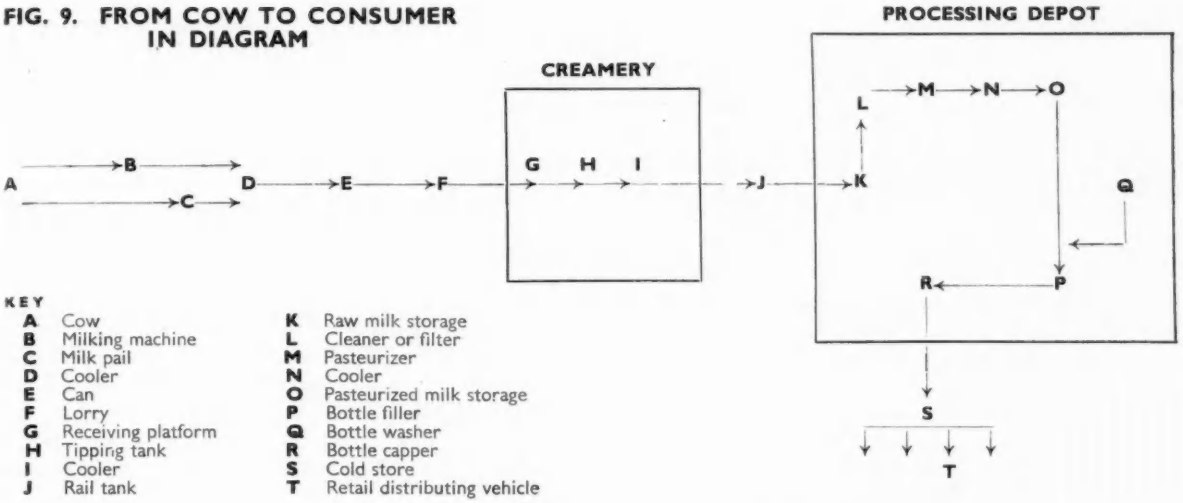


5. Bottling

The cold milk passes before bottling to storage-tanks, where it is kept in gentle agitation to prevent separation of cream, from whence it passes to the bottling-machines. The bottles, either new or as received back from the consumer, are washed and sterilized in mechanically-operated washers capable of handling up to 160 bottles per minute (fig. 7).

They first receive a rinse with tepid water to remove residues of milk or any loose material which may have gained access. They are then treated externally and internally with hot caustic-soda solution, either by complete immersion in the solution or spraying from jets under pressure, or a combination of both. The objects of this treatment are to dissolve any material not previously removed by the water-rinse, and to effect sterilization, as for the latter purpose steam cannot be applied for the requisite time where large numbers of bottles have to be treated. The combination of time, temperature, and concentration of caustic soda necessary to attain this object is illustrated

FIG. 9. FROM COW TO CONSUMER IN DIAGRAM



KEY

A	Cow	K	Raw milk storage
B	Milking machine	L	Cleaner or filter
C	Milk pail	M	Pasteurizer
D	Cooler	N	Cooler
E	Can	O	Pasteurized milk storage
F	Lorry	P	Bottle filler
G	Receiving platform	Q	Bottle washer
H	Tipping tank	R	Bottle capper
I	Cooler	S	Cold store
J	Rail tank	T	Retail distributing vehicle

in the table given by Hobbs & Wilson (1943). In practice, temperatures of 140-150°F. are usual, and concentrations of caustic soda at least double (i.e. 2-3%) those given by Hobbs & Wilson in order to provide an ample margin of safety. The caustic-soda treatment is followed by rinsing with clean water at decreasing temperatures to remove the caustic solution and cool the bottles so that they emerge at about 60°F. or less. In order to obtain free rinsing, it is usual at some stage to incorporate an alkali phosphate, such as trisodium phosphate or sodium hexametaphosphate, or one of the newer organic wetting-agents.

At the discharge-end, the bottles are visually inspected and any containing foreign material such as cement, bottle-caps, etc., which cannot be dealt with by the caustic soda, are removed. It is possible that in the near future this inspection may become automatic.

From the washing-machine the bottles immediately pass along covered conveyors to the completely automatic bottling-machines capable of filling up to 4,800 bottles per hour with the cold milk from the storage tanks. Adjacent to each bottling machine is a capping machine which inserts a waxed cardboard disc in the mouth, or clinches on an aluminium cap which has been cut from a strip as the bottle passes to the capping-head. Fig. 8 shows such a completely automatic combined filler and capper. The advantage of the aluminium cap is that the pouring-lip is protected from any contamination during the handling which is unavoidable between this stage and delivery to the customer—the first occasion on which there is again a possibility of contamination in the long journey from the cow to the home.

The filled bottles are packed into clean crates which are immediately transported to cold-stores, whence the milk goes out on the rounds for delivery to the customer's doorstep.

6. Care in the Home

As all consumers cannot be supplied with safe milk of good keeping-quality,which results from the procedure described, it is desirable to refer here to the procedure to be adopted where the size of the community does not allow of the economic distribution of pasteurized milk, and where, therefore, raw milk has to be consumed. Where available, TT (Tuberculin Tested) milk should be used, as this is reasonably safe, but where it is not, or where young children are concerned, all raw milk should be brought just to the boil before use, and after transfer to a clean vessel cooled by standing in cold water, the mouth of the container should be covered with a loose metal or net cap to prevent access by flies, etc.

All milk should be kept as cool as possible at all times, preferably in a refrigerator. Where larders are unsuitably situated and refrigerators non-existent, covering the bottles with one of the porous-clay covers filled with water made for this purpose is a very useful method, or alternatively, keeping the bottles in an outside meat-safe fixed to a north wall. The mouth of the bottles should always be kept covered when not in use, to prevent attention by cats and other vermin. Milk should not be exposed to sunlight as, apart from the heat-effect, this causes rapid destruction of the vitamin C, and, at certain seasons of the year, the development of an objectionable flavour in the cream referred to usually as 'cardboard,' 'powdery,' etc.

When empty, the bottle should be rinsed out with cold, not hot water, as residues of milk left in bottles standing on doorsteps and similar places attract flies, snails and other undesirable visitors, and make the eventual cleaning far more difficult than it should be.

Finally, milk-bottles should never be used as containers for paraffin, disinfectants or similar materials.

* * * *

To sum up, the outstanding developments during the last 25 years have been :—

i. Application of the principles of hygiene on the dairy farms, and increased attention to the health of the animals.

ii. Refrigeration and bulk-transport.

iii. Pasteurization or equivalent heat-treatment of the milk supplied to the larger communities.

iv. Reduction of contact with the human hand to a minimum by increased mechanization and the use of bottles.

v. Improved methods and a higher standard of cleaning and sterilization of creamery and processing plants.

Continued at foot of page 214

LACTATION AND ITS PRODUCTS

A Bibliography of British Books and Journals

W. G. SUTTON M.Sc. A.R.I.C

Director, Imperial Bureau of Dairy Science
Shinfield, Reading

The literature in which our knowledge of milk and its products is recorded is both large and scattered. Information of a scientific sort is commonly recorded first in a periodical. It is true that in Britain we have a few periodicals devoted entirely to dairying, but we have many more which from time to time publish articles dealing with milk among more numerous articles dealing with other subjects. Books tend to be more specialized, but even at this stage considerable scattering persists. This scattering of information results in difficulty in knowing where to seek needed facts; this in turn results in ignorance from unwillingness or inability to find them. Every argument on pasteurization of milk demonstrates these results.

Medical men are much concerned with lactation in the human and with utilization of milk by the human. In our civilization, most of the milk used by mankind is obtained from the domesticated animals. The production, processing, distribution and control of the very large quantities of perishable food involved constitute one of our greatest industries. The belief that this farming, processing and distributing industry is not well understood by consumers and their medical advisers is the excuse for the inclusion in this bibliography of so many periodicals and books outside the normal range of interest of medical men. It is hoped that sufficient information is given to open, for those who so desire, the gate to a wide and cultivated field.

A. PERIODICALS

The data given are name of the publication, frequency of appearance, place of publication, name of publisher, amount of annual subscription.

1. Specialized journals in the field of dairying and dairy science.

The dairy farmer. Monthly. Ipswich: Dairy Farmer. Eight shillings. [£0.4]

News, opinion and discussion for the milk producer.

Dairy industries, incorporating ice cream manufacture and dairy technology. Monthly. London: Dairy Industries. Twenty shillings. [£1]

This journal circulates widely in the milk-processing and dairy manufacturing industry: it publishes short papers describing investigations in applied dairy-science, articles furthering the application of scientific knowledge in the industry, and news.

The dairyman. Monthly. London: Dairyman. Ten shillings and sixpence. [£0.525]

News, opinion and discussion for the milk-distributor.

Dairy science abstracts. Quarterly. Shinfield, Reading: Imperial Bureau of Dairy Science. Twenty-five shillings. [£1.25]

The Imperial Bureau of Dairy Science attempts in this journal to abstract all current research on milk and milk-products. The field includes dairy husbandry, technology, legal control, economics, physiology of lactation, nutritive value of milk and its products, bacteriology and mycology, chemistry and physics. The journal is linked with *Animal Breeding Abstracts, Herbage Abstracts, Nutrition Abstracts and Reviews* and *The Veterinary Bulletin.*

The journal of dairy research. Irregular. London: Cambridge University Press. Twenty-five shillings [£1.25] (per volume of three issues).

Essentially a journal for the publication of original research from the British Commonwealth, but each issue includes a valuable and authoritative review of the progress of dairy-science. Formerly the journal appeared three times yearly, and sections of the subject were reviewed each two years.

The journal of the Society of Dairy Technology. Quarterly. London: Society of Dairy Technology.

A new journal. The first issue appeared in October 1947. It is essentially the proceedings of the Society and contains a selection of papers read and discussions thereon.

The milk industry. A progressive journal devoted to the production and distribution of milk. Monthly. London: National Dairymen's Association. Ten shillings. [£0.5]

Essentially a news journal for distributors of liquid milk.

2. Agricultural journals containing useful information in the field of dairying.

Agricultural progress. The journal of the Agricultural Education Association. Twice yearly. Shrewsbury: Wilding & Son. Five shillings. [£0.25]

Papers read before the Dairying Section of the Agricultural Education Association are published; they are intended to be of interest to agricultural advisers and teachers.

Agricultural statistics, Ministry of Agriculture and Fisheries. Part I. Acreage and production of crops, number of live stock and of agricultural workers, and output and prices of agricultural produce in England and Wales. Part II. An analysis of agricultural production, prices and supplies in England and Wales. Twice yearly. London: His Majesty's Stationery Office. Price variable.

The latest issue, Part I of the volume dealing with 1939, appeared in 1941. Official statistics concerning milk-production.

Agriculture. The journal of the Ministry of Agriculture. Monthly. London: His Majesty's Stationery Office. Eight shillings. [£0.4]

Mildly informative articles for the farmer.

Animal breeding abstracts. Quarterly. Edinburgh: Imperial Bureau of Animal Breeding and Genetics. Twenty-five shillings. [£1.25]

Abstracts covering the field of animal breeding and animal production as related to breeding or heredity.

Continued from page 213

HANDLING AND DISTRIBUTION OF MILK

vi. Increase in the size of the units operating, with consequent reduction in the costs of operation.

vii. The introduction of stainless steel for the fabrication of plants wherever possible.

viii. The extension of laboratory control.

ACKNOWLEDGEMENTS

The photographs accompanying this article are reproduced by permission of the following firms: Aluminium Plant & Vessel Co. Ltd.; Mickleover Transport Ltd.; U.D. Engineering Co. Ltd.

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Hobbs, B. C. & Wilson, G. S. (1943) *J. Hyg., Camb.* **43**, 96
Kay, H. D. & Graham, W. R. (1935) *J. Dairy Res.* **6**, 191

The Ayrshire Cattle Society's journal. Quarterly. Ayr: Ayrshire Cattle Herd Book Society.

British agricultural bulletin. Quarterly. London: British Council. Ten shillings. [£0.5]
This is a new journal. The first issue is due to appear in November 1947. It will publish review articles on recent advances in british agricultural science and practice.

The British Friesian journal. Monthly. London: British Friesian Cattle Society. Six shillings. [£0.3]

British Goat Society monthly journal. Monthly. Diss: British Goat Society. Twelve shillings. [£0.6]

The British Goat Society's yearbook. Annual. Diss: British Goat Society. Three shillings. [£0.15]

The empire journal of experimental agriculture. Quarterly. London: Oxford University Press. Twenty shillings. [£1]
Original research.

The farm economist. Irregular. Oxford: Agricultural Economics Research Institute. One shilling. [£0.05]
Brief reports of investigational work. Bibliography of agricultural economics.

Farm economics. Miscellaneous notes on the economics of farming in Scotland. Twice yearly. Edinburgh: His Majesty's Stationery Office.

Farmer and stock-breeder. Weekly. London: Farmer and Stock-Breeder. Twenty-six shillings. [£1.3]
News, opinion and discussion for the farmer.

The farmers weekly. Weekly. London: Hulton Press. Twenty-eight shillings and twopence. [£1.4]
News, opinion and discussion for the farmer.

Goats. Monthly. Colchester: Trinity Printing Works. Seven shillings. [£0.35]

Guernsey breeders' journal. Quarterly. London: English Guernsey Cattle Society. Eight shillings. [£0.4]

Herbage abstracts. Quarterly. Aberystwyth: Imperial Bureau of Pastures and Field Crops. Twenty-five shillings. [£1.25]
Abstracts covering pastures and forage crops.

The home farmer. The journal of the Milk Marketing Board. Monthly. Thames Ditton: Milk Marketing Board.

The Jersey cow. Official journal of the English Jersey Cattle Society. Quarterly. London: English Jersey Cattle Society.

The journal of agricultural science. Quarterly. London: Cambridge University Press. Thirty shillings. [£1.5]
Original research.

Journal of the British Dairy Farmers' Association. Irregular. London: British Dairy Farmers' Association.

Journal, Department of Agriculture, Eire. Twice yearly. Dublin: Stationery Office. Three shillings. [£0.15]

Journal of the Farmers' Club. Irregular. London: Farmers' Club.
Addresses on topical subjects delivered to the Club, with discussion thereon.

The journal of the Red Poll breed. The official organ of the Red Poll Cattle Society of Great Britain and Ireland. Three times yearly. Ipswich: Red Poll Cattle Society of Great Britain and Ireland.

Journal of the Royal Agricultural Society of England. Annual. London: Murray. Five shillings. [£0.25]
Contains a review each year of dairy-farming and dairy-work.

The Manx journal of agriculture. Quarterly. Douglas: Board of Agriculture and Fisheries. Four shillings. [£0.2]

Monthly report, Ministry of Agriculture, Government of Northern Ireland. Monthly. Belfast: His Majesty's Stationery Office.

Proceedings of the Society for Applied Bacteriology (formerly *Society of Agricultural Bacteriologists*). Twice yearly. (No permanent address): Society for Applied Bacteriology.
Many short papers on dairy-bacteriology appear in this journal. The journal has changed its name with the name of the Society; further it formerly described itself as *Abstracts*. Before 1946 it appeared annually.

Scottish agriculture. The journal of the Department of Agriculture for Scotland. Quarterly. Edinburgh: His Majesty's Stationery Office. Four shillings. [£0.2]

The Scottish farmer and farming world and household. Weekly. Glasgow: Scottish Agricultural Publishing Co. Twenty shillings. [£1.0]
News, opinion and discussion for the farmer.

The Shorthorn journal. Incorporating the Dairy Shorthorn journal. Monthly. London: Shorthorn Society of the United Kingdom of Great Britain and Ireland. Six shillings. [£0.3]

Transactions of the Highland and Agricultural Society of Scotland. Annual. Edinburgh: Blackwood. Five shillings. [£0.25]

The Welsh journal of agriculture. The journal of the Welsh Agricultural Education Conference. Annual. Cardiff: University of Wales Press Board. Two shillings and sixpence. [£0.125]
Original investigations into welsh agriculture.

3. Veterinary journals containing useful information in the field of dairying.

Index veterinarius. Twice yearly. Weybridge: Imperial Bureau of Animal Health. One hundred shillings. [£5.0]
A classified list of references to current publications of veterinary science.

The journal of comparative pathology and therapeutics. Quarterly. Croydon: Grubb. Thirty shillings. [£1.5]
Original work.

The veterinary bulletin. Monthly. Weybridge: Imperial Bureau of Animal Health. Forty shillings. [£2.0]
Abstracts in the field of animal health.

The veterinary journal. Monthly. London: Baillière, Tindall and Cox. Thirty shillings. [£1.5]
Original work.

Veterinary record. Weekly. London: National Veterinary Medical Association of Great Britain and Ireland. Seventy-eight shillings. [£3.9]
Original investigations; news and opinion for members of the Association.

4. Medical journals containing material concerning milk and lactation.

Archives of disease in childhood (*incorporating the British journal of children's diseases*). Quarterly. London: British Medical Association. Twenty-five shillings. [£1.25]

The British journal of dermatology and syphilis. Six times yearly. London: Lewis. Forty-two shillings. [£2.1]
Reports of cheese-mite itch.

The British journal of experimental pathology. Six times yearly. London: Lewis. Forty shillings. [£2.0]

The British journal of tuberculosis and diseases of the chest. Quarterly. London: Baillière, Tindall and Cox. Fifteen shillings. [£0.75]

British medical bulletin. Irregular. London: British Council. Twenty shillings. [£1.0]

The British medical journal. The journal of the British Medical Association. Weekly. London: British Medical Association. Sixty-seven shillings. [£3.35]
Original investigations; news and discussion for members of the Association.

Bulletin of hygiene. Monthly. London: Bureau of Hygiene and Tropical Diseases. Thirty shillings. [£1.5]
An abstracting journal with an occasional article reviewing some aspect of hygiene; covers the public-health aspect of milk.

The bulletin of the Institute of Medical Laboratory Technology. Six times yearly. London: Institute of Medical Laboratory Technology. Fifteen shillings. [£0.75]

Publishes an occasional minor article on laboratory technique concerned with milk.

Edinburgh medical journal. Monthly. Edinburgh: Oliver and Boyd. Forty shillings. [£2.0]

The Glasgow medical journal. Monthly. Glasgow: Royal Medico-Chirurgical Society of Glasgow. Forty shillings. [£2.0]

The Irish journal of medical science. Monthly. Dublin: Cahill. Twenty shillings. [£1.0]

The journal of hygiene. Irregular. London: Cambridge University Press. Seventy-five shillings [£3.75] (per volume of six issues).

Publishes original work on dairy bacteriology and public-health aspects of milk.

The journal of pathology and bacteriology. The official journal of the Pathological Society of Great Britain and Ireland. Quarterly. Edinburgh: Oliver and Boyd. Sixty shillings. [£3.0]

Journal of the Royal Army Medical Corps. Monthly. London: Staples. Thirty shillings. [£1.5]

The journal of the Royal Institute of Public Health and Hygiene. Monthly. London: Gerrans. Twenty-four shillings. [£1.2]

Journal of the Royal Sanitary Institute. Quarterly. London: Royal Sanitary Institute. Fifteen shillings. [£0.75]

The journal of tropical medicine and hygiene. Six times yearly. London: Bale Medical Publications. Fifteen shillings. [£0.75]

The lancet. A journal of British and foreign medicine, surgery, obstetrics, physiology, pathology, pharmacology, public health, and news. Weekly. London: Lancet. Forty-two shillings. [£2.1]

The medical officer. A journal for medical men in the government and municipal services. Weekly. London: Hodgetts. Fifty-two shillings and sixpence. [£2.625]

Monthly bulletin of the Ministry of Health and the Public Health Laboratory Service. Monthly. London: Ministry of Health.

From time to time publishes articles dealing with milk and public health, including accounts of epidemics spread by milk and dairy-products.

Proceedings of the Royal Society of Medicine. Monthly. London: Longmans, Green. One hundred and five shillings. [£5.25]

Public health. The journal of the Society of Medical Officers of Health. Monthly. London: Society of Medical Officers of Health. Thirty-one shillings and sixpence. [£1.575]

Quarterly journal of experimental physiology and cognate medical sciences. Irregular. London: Griffin. Forty-two shillings (per volume). [£2.1]

Original researches.

Transactions of the Ophthalmological Society of the United Kingdom. Annual. London: Ophthalmological Society of the United Kingdom. Forty shillings. [£2.0]

Galactose cataract.

Transactions of the Royal Society of Tropical Medicine and Hygiene. Six times yearly. London: Royal Society of Tropical Medicine and Hygiene. Thirty-five shillings. [£1.75]

Tubercle. Monthly. London: Bale Medical Publications. Thirty-five shillings. [£1.75]

5. Journals of fundamental and applied science in which dairy science is published.

The analyst. The journal of the Society of Public Analysts and other Analytical Chemists. Monthly. Cambridge: Heffer and Sons. Thirty-five shillings. [£1.75]

Original investigations and abstracts in the field of chemical analysis and microbiological assay.

Annual reports of the Society of Chemical Industry on the progress of applied chemistry. Annual. London: Society of Chemical Industry. Eleven shillings and sixpence. [£0.575]

Annual reports on the progress of chemistry. Annual. London: Chemical Society. Fifteen shillings. [£0.75]

The biochemical journal. Irregular. London: Cambridge University Press. Seventy shillings. [£3.5]

Original research, including work on the biochemistry of milk, milk-secretion, and the nutritive value of milk.

Biological reviews of the Cambridge Philosophical Society. Quarterly. London: Cambridge University Press. Forty-two shillings. [£2.1]

British abstracts. AI. General, physical, and inorganic chemistry. Monthly. Fifty-five shillings. [£2.75] *AII. Organic chemistry.* Monthly. Fifty-five shillings. [£2.75] *AIII. Physiology, biochemistry, anatomy.* Monthly. Eighty shillings. [£4.0]. *BI. Chemical engineering and industrial inorganic chemistry, including metallurgy.* Monthly. Fifty-five shillings. [£2.75]. *BII. Industrial organic chemistry.* Monthly. Fifty-five shillings. [£2.75] *BIII. Agriculture, foods, sanitation.* Monthly. Thirty-five shillings. [£1.75]. *C. Analysis and apparatus.* Six times yearly. Fifteen shillings. [£0.75]. London: Bureau of Abstracts.

The British food journal and hygienic review. Monthly. London: British Food Journal. Eighteen shillings and sixpence. [£0.925]

A trade journal for the food-processing industry.

The British journal of nutrition. Quarterly. London: Cambridge University Press. Sixty shillings. [£3.0]

This is a new journal. The first issue appeared in September 1947. It contains original work in nutrition and the proceedings of the Nutrition Society.

Chemistry and industry. Weekly. London: Society of Chemical Industry. Fifty-five shillings. [£2.75]

Food. Processing-packing-marketing, with which is incorporated the canning and food trade journal. Monthly. London: Nema Press. Twelve shillings. [£0.6]

Food manufacture, incorporating food industries weekly. Monthly. London: Leonard Hill. Twenty shillings. [£1.0]

Index to the literature of food investigation. Quarterly. London: His Majesty's Stationery Office. Eighteen shillings. [£0.9]

Annotated references to, and abstracts of, scientific publications concerning processing, manufacture, storage, etc., of food.

The industrial chemist and chemical manufacturer. Monthly. London: St. Margaret's Technical Press. Twelve shillings. [£0.6]

Journal of anatomy. Quarterly. London: Cambridge University Press. Forty shillings. [£2.0]

Journal of the Chemical Society. Monthly. London: Chemical Society. Seventy-five shillings. [£3.75]

The journal of endocrinology. Irregular. London: Cambridge University Press. Thirty-five shillings [£1.75] (per volume of four issues).

Original research on the endocrinology of lactation.

The journal of physiology. Irregular. London: Cambridge University Press. Forty-five shillings. [£2.25]

The journal of the Royal Society of Arts. Twenty-six times yearly. London: Bell and Sons. Sixty-three shillings. [£3.15]

Lectures to the Society on general topics have included dairy-education, physiology of lactation, nutritive value of milk and milk-products, the dairy-industry, etc.

Journal of scientific instruments. A publication dealing with their principles, construction and use, and the applications of physics in industry. Monthly. London: Institute of Physics. Forty shillings. [£2.0]

Journal of the Society of Chemical Industry. Monthly. London: Society of Chemical Industry. Thirty-five shillings. [£1.75]

Original work on the chemistry of milk and milk-products.

Monthly digest of statistics. Monthly. London: His Majesty's Stationery Office. Thirty-two shillings and sixpence. [£1.625]

Official statistics of production, manufacture, imports, utilization, etc., of milk and milk products.

Nature. Weekly. London: Macmillan. Ninety shillings. [£4.5]

Nutrition abstracts and reviews. Quarterly. Bucksburn, Aberdeen: Imperial Bureau of Animal Nutrition. Forty-two shillings. [£2.1]

Abstracts covering the whole field of both human and animal nutrition, with an authoritative review-article in each issue.

Proceedings of the Nutrition Society. Quarterly. Cambridge: Heffer and Sons. Twenty-five shillings. [£1.25]

This journal will be superseded by *The British journal of nutrition* (see above).

Proceedings of the Royal Society. Series B. Biological sciences. Irregular. London: Cambridge University Press. Thirty-two shillings [£1.6] (per volume).

The scientific proceedings of the Royal Dublin Society. Irregular. Dublin: Royal Dublin Society.

Transactions of the Faraday Society. Monthly. London: Faraday Society. Sixty shillings. [£3.0]

Transactions of the Institution of Chemical Engineers. Annual. London: Institution of Chemical Engineers.

B. BOOKS

This list has been limited, with one exception, to books published in 1930 or later years. Books dealing with science rarely have a useful life of more than fifteen years nowadays: the need to restrict the labour of compilation likewise suggested such a limitation. Doubtless many even of these recent books are out of print. Unfortunately editions are so small and sell out so rapidly that it is quite impossible to give any indication of availability. Data given are author's name, title of the book, number of the edition, date and place of publication, publisher, price, whether illustrated or containing a bibliography.

1. Milk-production

a Dairy-farming

Cole, W. E. *Systems of dairy farming.* (College of Estate Management: Reports of the college travelling scholars in agriculture, No. 1.) 1st ed., 1930, London: College of Estate Management. (Printed for private circulation.) Illustrated. Bibliography.

The report covers the United Kingdom and the chief dairying countries of Europe.

Cookson, B. M. *Dairy cows and their management.* 1st ed., 1944, London: Faber and Faber. Five shillings. [£0.25] Illustrated.

A simple guide for beginners.

Duckham, A. N. *Animal industry in the British Empire. A brief review of the significance, methods, problems, and potentialities of the live-stock and dairying industries of the British Commonwealth.* 1st ed., 1932, Oxford: University Press. Fifteen shillings. [£0.75] Illustrated. Bibliography.

Fishwick, V. C. *Dairy farming. Theory and practice.* 1st ed., 1947, London: Crosby Lockwood. Fifteen shillings. [£0.75] Illustrated.

Half the book is devoted to descriptions by twenty farmers of their own farms and methods.

Foot, A. S. *Observations on American dairy husbandry.* (College of Estate Management: Reports of the college travelling scholars in agriculture, No. 5.) 1st ed., 1937, London: College of Estate Management. (Printed for private circulation.) Illustrated. Bibliography.

Garner, F. H. *British dairying.* 1st ed., 1946, London: Longmans, Green. Twenty-one shillings. [£1.05] Illustrated.

Gunn, E. *Farm buildings, new and adapted.* 2nd ed., 1945, London: Crosby Lockwood & Son. Ten shillings and sixpence. [£0.525] Illustrated. Bibliography.

Holmes, W. O'C. *Family goat keeping.* A "Goats" magazine handbook. 1st ed. [no date], Colchester: Trinity Printing Works. One shilling and sixpence. [£0.075] Illustrated.

Hoyland, A. *Machine milking. A bane or a boon?* 1st ed., 1939, London: Nicholls. Two shillings. [£0.1]

Robinson, H. G. *Good milk farming.* 1st ed., 1946, London: Hodder and Stoughton. Three shillings and sixpence. [£0.175] Illustrated.

b Feeding cattle

Ellis, J. C. B. *The feeding of farm live stock.* 1st ed., 1937, London: Crosby Lockwood. Fifteen shillings. [£0.75] Illustrated.

Hall, A. D. *The feeding of crops and stock. An introduction to the science of the nutrition of plants and animals. Part 3. The nutrition of animals and man.* 3rd ed. (revised by J. Hammond), 1944, London: Murray. Four shillings. [£0.2] Illustrated.

Halnan, E. T. & Garner, F. H. *The principles and practice of feeding farm animals.* 1st ed., 1940, London: Longmans, Green. Fifteen shillings. [£0.75] Illustrated.

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An authoritative review of the evidence for and against pasteurization.

Notes on Contributors

MR. K. C. RICHARDSON is Reader in histology at University College, London. He was formerly Lecturer in anatomy in the University of Sydney. At present he is working in collaboration with Dr. Folley and his colleagues of the National Institute for Research in Dairying on the problem of the artificial induction of lactation in virgin goats.

DR. S. J. FOLLEY received his early training in the famous School of Chemistry at Manchester. As Mercer Scholar in Chemistry, he took a research degree in colloid chemistry, and then began research in physiological chemistry in the laboratory of H. S. Raper. He has been a member of the staff of the National Institute for Research in Dairying since 1932, and during the last ten years he has become widely known as one of the world's leading authorities on the endocrine control of lactation and reproduction. As a Rockefeller Foundation Fellow in 1938, he spent some time in the laboratory of the late Edgar Allen at Yale.

DR. H. D. KAY is director of the National Institute for Research in Dairying, and is also research professor of biochemistry to the University of Reading. He is a graduate of Manchester and of Cambridge. He studied biochemistry under Sir Arthur Harden at the Lister Institute, Sir F. G. Hopkins in Cambridge and Professer Franz Knoop in Freiburg, became a member of the staff of the Medical Unit at the London Hospital in 1925, and later professor of biochemistry in the University of Toronto. His earlier research work was mainly on oxidations in the animal body, on the metabolism of phosphorus compounds, on enzymes (particularly the phosphatases and the reversibility of enzyme-action), on egg-yolk proteins and on milk-secretion. He was responsible for a biochemical technique now used to assist diagnosis of certain bone-disorders and, with W. R. Graham, devised a method, now official in Britain and widely employed abroad, for determining the efficiency of pasteurization of milk. At the National Institute for Research in Dairying, since 1933, he has initiated and directed research on many of the fundamental problems associated with lactation. He is a Fellow of the Royal Society.

DR. F. H. MALPRESS worked during the war years as an associate of Dr. S. J. Folley at the National Institute for Research in Dairying. His published work deals with studies on the hormonal control of reproduction and lactation, with particular reference to the dairy animal. Dr. Malpress was recently appointed Lecturer in biochemistry at Queen's University, Belfast.

PROFESSOR F. G. YOUNG began his career in 1929 as Bayliss-Starling Scholar in biochemistry at University College, London. In 1933 he became honorary research assistant at the department of physiology, University of Aberdeen, and in 1934 research associate at the department of physiology at the University of Toronto, returning in the same year to University College, London, as assistant in the department of physiology, pharmacology and biochemistry. From 1936-1942 he was a member of the scientific staff of the Medical Research Council at the National Institute for Medical Research, London. He served as joint honorary secretary (1938-1942) of the Biochemical Society and was chairman (1942-1946) of the editorial board of the *Biochemical Journal*. In 1942 he was appointed professor of biochemistry in the University of London at St. Thomas's Hospital Medical School (1942-1945) and then at University College (1945-). He is the author of some seventy publications relating to the influence of hormones on metabolism, with particular reference to the relation of the pituitary gland to diabetes.

DR. MARGARET ROBINSON has taken a special interest in the study of lactation in women. She was educated at Queen's University, Belfast. In 1941, while working as an Assistant Medical Officer for Maternity and Child Welfare in Liverpool, her attention was drawn to the higher morbidity- and mortality-rates of bottle-fed as compared with breast-fed infants. On the assumption that failure of lactation in the

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mothers of bottle-fed infants was probably of endocrine origin, she consulted Dr. S. J. Folley (v. supra) and Prof. F. G. Young (v. supra) and has now been working for nearly three years on the effect of hormones on lactation in women. The Medical Research Council has given her a full-time grant, and the work is being carried out in the Maternity Units of St. Thomas's and University College Hospitals. Dr. Robinson is the author of several papers published since 1939 on breast-feeding and failure of lactation.

MISS JOSEPHINE BARNES is at present assistant in the Obstetric Unit at University College Hospital and assistant obstetrician and gynaecologist at the Elizabeth Garrett Anderson Hospital, London. She has specialized in obstetrics and gynaecology since 1939, and has held the appointment of graduate assistant in the Nuffield Department of Obstetrics and Gynaecology at the Radcliffe Infimary, Oxford, and first assistant in the Obstetric Unit at University College Hospital. She has carried out clinical research-work on oestrogens and on early human ova and embryos, and has recently published results on the use of pethidine in labour.

DR. S. K. KON is head of the department of nutrition at the National Institute for Research in Dairying, where he has worked since 1930. From 1924 to 1927 he was assistant to Dr. Casimir Funk at the Warsaw School of Hygiene, and between 1927 and 1929 held a Rockefeller Travelling Fellowship. He is Honorary General Editor of the *Proceedings of the Nutrition Society* and member of the editorial board of the *Biochemical Journal*. He has published numerous papers on various aspects of nutrition, and has been specially interested in the value of milk as food, in problems of nitrogen- and calcium-metabolism, and of the intestinal synthesis of vitamins.

PROFESSOR B. S. PLATT was the subject of a biographical note in this journal (*BMB*, **2**, 200) in 1944. Since then he has been a member of the UK delegation to the United Nations' Food and Agriculture Organisation Conference at Quebec (1945), the UK delegation to the second Food and Agriculture Organisation Conference at Copenhagen (1946) and the Special Advisory Committee on Nutrition to the Director-General. In 1946 he was appointed professor of nutrition at the University of London, and head of the department of nutrition at the London School of Hygiene and Tropical Medicine.

PROFESSOR ALAN MONCRIEFF is well-known as one of Britain's leading paediatricians, and is the first holder of the Nuffield Chair of Child Health in the University of London. He is a member of the staff of the Hospital for Sick Children, Great Ormond Street, London, and director of the Institute of Child Health which came into being there in January 1946. Professor Moncrieff is the author of many publications on paediatric subjects.

DR. HAROLD WALLER is superintendent medical officer to the Royal College of St. Katherine, Poplar, and paediatrician at the British Hospital for Mothers and Babies, Woolwich and at the Poplar Hospital. He is the author of *Clinical studies in lactation* (1938) and of papers on breast-feeding. He believes that a baby thrives best if successfully fed at its mother's breast and that mothers have been inadequately taught how to do this.

DR. JEAN M. MACKINTOSH has been Senior Assistant Medical Officer for Maternity and Child Welfare for the City of Birmingham since September 1943. She is also part-time Reader in the University Department of Child Health. Previously she held appointments as regional medical officer for maternity and child-welfare, City and County of Aberdeen and County of Kincardine (1938-1943), Assistant Medical Officer of Health for maternity and child-welfare, Stockport (1928-1938), and Assistant Medical Officer of Health and assistant school medical officer, Llanelly (1923-1928). She has published papers on anaemia in pregnancy and on infant-feeding.

PROFESSOR J. R. MARRACK was appointed chemical pathologist to the London Hospital in 1919 and Professor of chemical pathology in 1934. He has carried out investigations on the nature and reaction of antigens and antibodies and published *The chemistry of antigens and antibodies* (London, 1938; MRC Special Report Series, No. 230) and, jointly with Dr. (now Sir Phillip) P. N. Panton, a standard work on *Clinical pathology* (1945). He has also published a number of papers on antigen-antibody reactions and is, at present, engaged in research on various aspects of clinical pathology.

PROFESSOR J. H. BURN has previously contributed to the Bulletin a paper on "The testing of local anaesthetics" (*BMB* **816**), with which a note on his work was published.

DR. J. SMITH is Deputy Medical Officer of Health for the City of Aberdeen, a Lecturer in the public-health department of Aberdeen University, and the director of the Municipal and Regional Public Health Laboratory Services for the North-Eastern Area of Scotland. He has been much interested in the application of modern bacteriological technique to the elucidation of many problems connected with the epidemiology of infectious diseases. For instance, he was able to prove definitely that streptococcal infection in puerperal women is more frequently derived from exogenous than endogenous sources. His published work includes papers on the etiology of puerperal fever, new types of Salmonellas, the incidence of leptospiral infections in fish-workers, and the incidence and distribution of undulant fever.

MR. A. ROWLANDS is a member of the staff of the bacteriology department of the National Institute for Research in Dairying. Before his appointment to this post in September 1945, he was advisory bacteriologist and head of the bacteriology department at the Midland Agricultural College, a post which he occupied for a period of 17 years. Throughout his career he has been in close touch with the practical problems involved in controlling the bacteriological quality of milk through the stages of production, processing, and distribution. Mr. Rowlands has made a special study of methods of testing pasteurized milk, and the results of his investigations led to the adoption of the methylene-blue test for the official examination of pasteurized milk. During the summer of 1946, he visited the USA as a member of a mission appointed by the British Ministry of Agriculture to study methods of milk-production and control in North America.

MR. J. MCCLEMONT is a graduate in agricultural science of Glasgow University, and holds the National Diplomas in Dairying and Agriculture. After a short period on the staff of the West of Scotland Agricultural College he went to the National Institute for Research in Dairying as research assistant in dairy husbandry. In 1927 he was appointed to the post of adviser in dairy bacteriology on the staff of Reading University, and in October 1946 was transferred to the National Agricultural Advisory Service as specialist officer in bacteriology. Mr. McClemont's main interest has been the bacteriological control of milk. His published work includes papers on the accuracy of the plate (colony) control for milk and the influence of mastitis on the tests used in milk-control. As an adviser his work has consisted of the investigation of bacteriological problems arising during the production and handling of milk, and the interpretation of the results of dairy-research to the industry.

DR. J. G. DAVIS was formerly head of the section of bacterial metabolism at the National Institute for Research in Dairying. He is now a Director (Technical) of the Express Dairy Company, and also a Director of Industrial and Scientific Instruments Ltd. Dr. Davis has worked principally on the bacteriology and biochemistry of milk and milk-products, and especially on the lactic-acid bacteria, cheese-ripening, bacteriological tests for milk-mastitis, and bacteriological media. His present interests are in routine control-tests in the dairy-industry, new types of detergent, and new scientific instruments for the dairy- and food-industries. He has published a number of original papers on various aspects of dairying bacteriology, and is preparing a Dictionary of Dairying and a book on cheese.

MR. E. B. ANDERSON has had an extensive and varied experience of industrial chemistry. He spent five years as research chemist to John Power & Sons, Ltd., distillers, of Dublin—the first post of this nature in Ireland. For three years during the 1914-18 war he was in the nitroglycerine section of the Royal Gunpowder Factory, Waltham Abbey, and for five years a technical research chemist at the British Dyestuffs Corporation, Blackley, Manchester, in charge of a section on chrome-azo-dyes and their intermediates. A further five years was spent as chemist and manager of a creamery and spray-dried-milk plant in Devonshire, after which he was appointed to his present post of chief chemist to United Dairies, Ltd., and its sub-companies. In this capacity he is concerned with all the research and control work applied to milk and its products, i.e. butter, cheese, milk-powder, condensed and evaporated milks, milk-sugar, etc., and the general problems arising in any big manufacturing company. He is joint honorary secretary of the Society of Chemical Industry, and a member of several learned societies.

MR. W. G. SUTTON was formerly lecturer in dairy chemistry and dairy bacteriology at Massey Agricultural College, University of New Zealand. In 1938 he came to England to start the Imperial Bureau of Dairy Science, of which he is Director. The Bureau scans the world literature relating to milk and milk-products and distributes the collected information to dairy-scientists. Mr. Sutton edits the Bureau's journal *Dairy Science Abstracts* and is in a unique position to survey the literature of dairy-science.

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BRITISH MEDICAL BULLETIN
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PART TWO · COMMENTARY
HISTORY · DOCUMENTATION

IN previous volumes the Bulletin contained, in addition to the scientific symposium which occupied the greater part of each number, subsidiary sections of bibliographical and historical interest. Starting with the first number of Volume 5, the Bulletin has been clearly divided into two parts. The collective monograph on a special subject which had become the characteristic feature of the Bulletin now constitutes Part I. Part II contains miscellaneous articles on medical subjects of scientific, bibliographical, and historical interest. The book-review section is extended and there are, as before, sections devoted to historical notes, film-reviews, and lists of contents of current british medical and cognate periodicals. It is our intention that Part II should be a medium for extending the range of interest of each number of the Bulletin and for enhancing its continuity as a periodical.

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Guide to the Journals

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ROBERT STENHOUSE WILLIAMS AND THE ORIGIN AND EARLY DEVELOPMENT OF THE NATIONAL INSTITUTE FOR RESEARCH IN DAIRYING

H. F. BURGESS A.C.I.S.

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The early history of the National Institute for Research in Dairying is largely a chapter in the biography of one man—Robert Stenhouse Williams—whose energy and vision motivated and guided its development from its beginnings as a very small team of research-workers to a well-established institute with an international reputation. He was himself essentially a modest man, and one who had the welfare of his fellow-creatures very much at heart. He had a large vision of his work, which he saw as a contribution to the betterment of mankind. As a medical man he realized its relation to human health, and he fought for his ideals persistently and courageously, yet with patience and forbearance, and with due appreciation of the other man's point of view.

Thorough in all he did, he looked for the same quality in his staff, to whom he was loyal and devoted, as were they also to him. Never inclined to take credit to himself, he was always concerned to ensure that full credit should go to the members of his staff. His relations with them were almost paternal, and were reflected in innumerable acts of kindness and consideration. Outside the Institute he was tireless in his efforts to give help and advice wherever they were needed. He was altogether a remarkable and lovable personality.

Robert Stenhouse Williams was born in Liverpool in 1871, and was the son of a medical man. After qualifying in medicine and surgery at Edinburgh University, he returned to Liverpool as Assistant Bacteriologist in the Public Health Department of the University. He also held several lectureships on public health and bacteriology in Liverpool, as well as hospital appointments. He worked also for a period in the laboratory of Professor Weinberg at the Pasteur Institute. He had thus acquired a thorough training in bacteriology and a wide experience in the practical applications of the science which were to prove an excellent preparation for his life's real work, on which he entered in 1912.

Beginnings of the Institute

In that year, two senior posts—Research Bacteriologist in Dairying, and Research Chemist in Dairying, were created at University College, Reading (now the University of Reading), by the aid of a grant from the Development Fund. That fund had been established in 1909 with the object, among others, of aiding and developing british agriculture and, as part of the plan for achieving that object, centres of research were established in various parts of the country. The two posts at Reading constituted the modest provision made initially for dairying. Stenhouse Williams was appointed Research Bacteriologist, and the post of Research Chemist went to the late John Golding, who came to Reading from the Midland Agricultural College.

The Institute thus started with two members of staff. Its income was of the order of £2,000 per annum, of which rather less than half was absorbed by salaries. The remainder had to cover maintenance-costs, and the facilities which could be provided for the work were correspondingly modest. The Institute was housed in part of a private dwelling-house, and its accommodation was very inconveniently distributed between attic and cellar.

The first task of the newly-appointed staff was to create laboratories. Two or three attic-rooms, and one room in the cellar, were adapted to this purpose. Another attic-room contained the nucleus of the library, mainly Stenhouse Williams' own collection of books. A small assistant staff was also appointed, consisting of two laboratory assistants, and a graduate "Assistant for Publications" who, in addition to having charge of the "library", was also responsible for the clerical work.

The Institute had no cows and no experimental dairy of its own, and it depended on the co-operation of those in charge of the College Farm and the British Dairy Institute in the conduct of experiments on milk-production and on the preparation of dairy-products. Stenhouse Williams was always generous in his tributes to the help he received from these sources, but it was obvious that such help could be only very limited. The farm and dairy were primarily teaching-centres, and their resources were barely sufficient for that purpose.

It was thus evident almost from the start that the work of the Institute would be handicapped until it had a farm and dairy under its own control, and it did in fact suffer from that handicap for seven years.

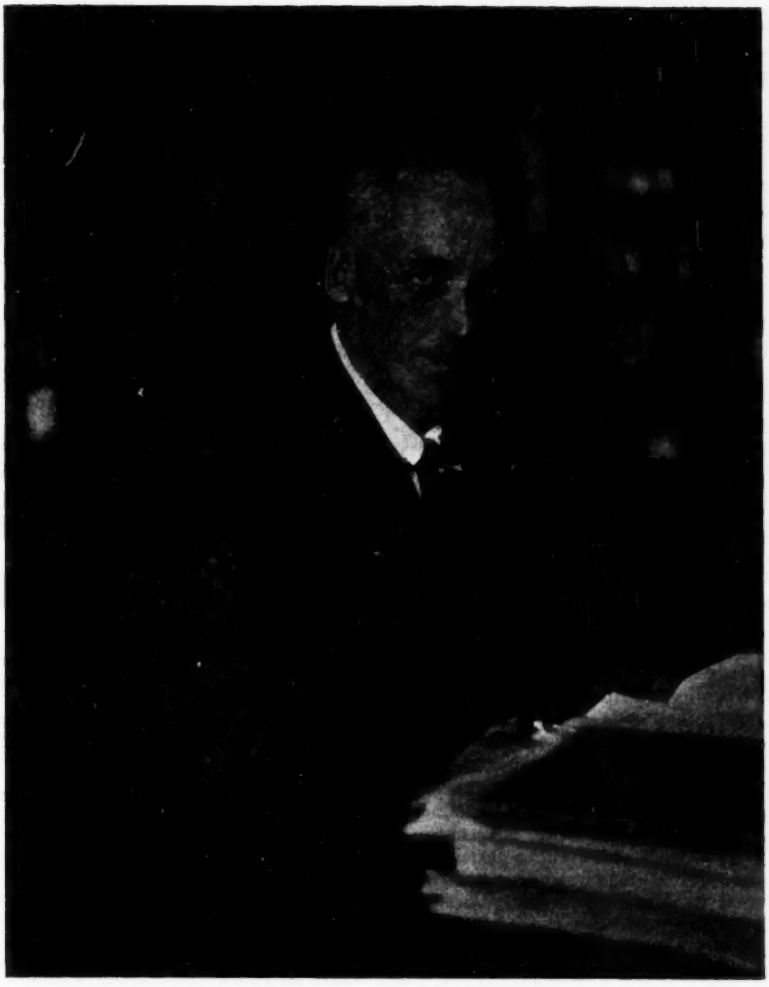
But the lack of all but the bare minimum of facilities for the study of the problems of the dairy-industries was matched by an almost complete lack of information about those problems, and the only line of attack appeared to be to carry out such work as came to the laboratory, and to gather information as time progressed.

Early Studies

One of the earliest studies was developed from the work of John Golding at the Midland Agricultural College on the discoloration of Stilton cheese. Further study at the Institute demonstrated that this fault was primarily due to dirt-organisms in the original milk. A survey of the conditions under which the milk was being produced led to the study of the methods of milk-production—a study which was to form the basis of the work of the Institute for some time to come, and which was to play an important part in the development of what came to be known as the clean-milk campaign.

It is perhaps difficult in these days to realize the nature and fundamental importance of the truly pioneering work carried out by Stenhouse Williams and his colleagues in the course of

this campaign. The conditions under which milk is produced and handled have been so improved, largely as a result of the efforts of themselves and their collaborators, that the difficulties with which they had to contend are apt to be forgotten. Conditions on many farms were primitive. Water-supplies were dirty and inefficient, cows were living and milk was being produced under insanitary conditions. In many cases no consideration was given to the cleanliness of the cows or of the milkers. Even on the better farms, where buildings and other facilities were of a higher standard, there was still a lack of understanding of how to make the best use of them. Methods of production and handling left much to be desired. The management of the milk at the receiving depots was equally unsatisfactory, where very little attention was given to the adequate cleaning and sterilization of the churns.



ROBERT STENHOUSE WILLIAMS 1871–1932

Founder of the National Institute for Research in Dairying

Stenhouse Williams and his colleagues were able to demonstrate that these conditions were the cause of very considerable losses to the industry, and they were further able, as a result of a long series of experiments, to suggest remedies. But there was no economic inducement to the farmer to apply those remedies, and much apathy and misunderstanding had to be overcome. Furthermore, the importance of milk as a foodstuff in the national dietary was not fully realized even by the medical profession. A further cause of the unsatisfactory state of the industry was inadequate technical education, for which the lack of well-equipped dairy-schools was partly responsible. There was no provision for practical instruction in proper methods of milk-production, and no collaboration between the production of milk in the cowshed and the preparation of dairy-products in the dairy-school. The improvement of dairy-education was, then, another of the objectives which Stenhouse Williams set himself to help to achieve, partly by means of Clean Milk Competitions and partly by arranging lectures and demonstrations at the Institute for those engaged in dairy-teaching, and by undertaking a considerable burden of lecturing.

Two other important lines of research were started in these early years, the study of acidity in relation to dairy-products and of the viability of the tubercle bacillus on pasture-land. In connexion with the latter experiment, the Institute rented a small piece of pasture-land with a small wooden shed where two or three cows excreting tubercle bacilli in their faeces were kept for study. These were cared for by a lady who, it is amusing to note, is described in an early record of those days, as "Assistant in charge of farm".

The War-period: 1914-1918

In 1914, it appeared as though the work would be stifled by the outbreak of war. John Golding and his two laboratory assistants joined the Army, and until Golding's return in 1919, Mrs. E. C. V. Mattick, who had been a Ministry of Agriculture Research Fellow at the Institute, undertook the supervision of the chemical laboratory.

Nevertheless, an important development took place during the war-period for, in 1916, a small Committee of persons interested in the Institute was formed under the Chairmanship of the late Ernest Mathews to act in collaboration with the College in developing the Institute. The Committee had two main objectives: (i) to remove the severe handicaps imposed on the work by lack of adequate laboratories and a farm and dairy and (ii) to obtain more definite knowledge

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than had hitherto been available of those problems of the industry calling for scientific investigation. The immediate pursuit of the first objective was rendered difficult by the war. The second had in some ways been rendered more urgent by the war. A Sub-Committee was appointed to conduct an inquiry into the extent of the losses incurred by the milk- and dairy-industries through bad methods of milk-production and -distribution. Its findings confirmed and extended the conclusions on this matter derived from the work on the discoloration of Stilton cheese, and led to a study of losses due to faulty handling and distribution of milk, and to the publication of a series of papers on sources of contamination and methods of prevention.

Thus, the main lines of work tended to develop in three directions: the production, handling, and distribution of milk; the importance of acidity in dairy-products; and the prevention of disease in cattle, a development of the original work on tuberculosis.

These researches took the staff into the field and brought them into direct touch with the milk-producer and -distributor. Stenhouse Williams himself established contacts which were to develop into lasting friendships and to gain many enthusiastic supporters for his work. In this way also the Committee was assisted in its efforts to bring the needs of the Institute to the notice of those whom it was intended to serve.

The National Institute Founded

As soon as the war was over, an Appeal Committee was formed under the chairmanship of the present Earl of Iveagh, and the campaign for raising funds was intensified.

In 1920, a new chapter in the history of the Institute was opened. John Golding had returned in the previous year to resume his post as Research Chemist, and the staff had been further strengthened by the appointment of James Mackintosh as Head of a Section of Dairy Husbandry, created in anticipation of the acquisition of a farm and dairy.

The Appeal Committee had collected funds sufficient, with grants from the Development Fund and generous help from Lord Iveagh, to purchase the Shinfield Manor Estate of some 357 acres[1]. At the same time, the government of the Institute was delegated, by Deed of Trust executed by University College, Reading, to an independent Board comprising representatives of the College, the Ministry of Agriculture, the Ministry of Health, the Royal Agricultural Society of England, the National Farmers' Union, the British Dairy Farmers' Association, the Staff of the Institute, and individual subscribers to the Trust funds and others interested in the milk industries. At this time, also, the title of the Institute was changed to the "National Institute for Research in Dairying". With the establishment of the Board, the old Committee of Dairy Research came to an end.

The primary objects of the Trust were to ensure that monies and other property given for the purposes of the Institute should be legally secured for those purposes, to give the governing board a large measure of autonomy, and by these means to strengthen its hand in appealing to the public for additional funds. And additional funds were urgently needed, for although the Institute had acquired its farm, it was still lacking adequate buildings. The Manor House, which before acquisition by the Institute had been occupied as a private dwelling, had to be converted for use as laboratories; services of heat, light, power and water had to be provided. A dairy and some modern farm-buildings had to be erected.

The years 1920-23 were very much occupied in planning and erecting the new buildings. In the meantime, the laboratory work was continued in the original primitive laboratories. The new farm, however, was occupied in 1920, and in spite of the inadequacy of the buildings, much experimental work on the handling of whole milk and the preparation of dairy-products was carried out. An ill-lighted wooden cowshed with a thatched roof and bare earthen floor was "modernized" at a small cost by the provision of concrete floor and standings—the minimum provision necessary to enable the place to be kept clean—and here Stenhouse Williams and his colleagues were able to demonstrate that methods were of more importance than expensive housing and equipment in the production of clean milk. Another wooden shed was adapted as a dairy and cooling-room by the introduction of a concrete floor and the use of whitewash. All water for the cowshed and dairy had to be carted by hand from an ordinary well-pump.

These primitive buildings were preserved and used for some years to demonstrate what could be achieved under conditions which, at most, were no better than those to be found on the majority of british farms.

During this time, the Appeal Committee continued to be actively engaged in raising funds to pay for the new buildings. In this work, Stenhouse Williams played a leading part. He would take advantage of every opportunity to make known the needs of his Institute, and the financial records of those times bear testimony to his activities in the long lists of individual donations, ranging from a few shillings to several pounds, which he was personally instrumental in collecting. He was also able to demonstrate in a practical way how the Institute could help in solving the problems of the industry, and he valued even more than the financial support the widespread interest which was developed in the work of the Institute.

The problem of raising capital funds was not the only one confronting Stenhouse Williams and his supporters. A larger income was also needed, and in the stringent financial circumstances of 1920 it was very much a matter of cutting one's coat according to one's cloth. The total available income in that year was about £5,000, most of which was derived from Government grant, and the Minute books of the time show that several meetings of the Staff Committee were held to consider how to keep within the budget.

It appears that in the result the irreducible minimum of expenditure exceeded the income by about £250 !

The Professional Committee

It may be appropriate here to make further reference to the Staff Committee. This Committee, known as the Professional (Staff) Committee, was created very soon after the establishment of the Institute, at the instigation of Stenhouse Williams, and consisted of himself, his senior colleagues, and one or two collaborators on the Staff of University College. It was responsible broadly for the internal control and supervision of the work of the Institute. There was no Director in those days, the staff was very small, and the

[1] [1 acre = 0.4 hectare.—ED.]

relations between its members were in consequence personal and intimate. The Committee system of control appeared to be most appropriate to these circumstances and, moreover, accorded with Stenhouse Williams' own belief that the staff ought to share the credit for and the burdens of the development of the Institute. The Chairmanship of the Committee was an elective office, although he himself was invariably voted to the Chair.

In that position he regarded himself as first among equals, and for long he steadfastly set his face against the creation of the office of Director. It was only when his administrative duties became so heavy that he clearly could not combine them with the duties of Head of the Bacteriology Department, that, on pressure from his colleagues, who freely acknowledged his leadership, he accepted the title of Director. He was largely influenced in this decision by his recognition of the fact that in fairness to the colleague who was in factual control of the Bacteriology Department, he himself could no longer continue to be titular head.

The Professional Committee, however, continued in being under the Chairmanship of the Director. Its governmental functions have been absorbed by the Board or vested in the Director, but it still performs important advisory functions.

In 1923, the Institute completed its move to its new home. By this time, the staff had been organized in three main departments—Bacteriology, under Stenhouse Williams, Chemistry, in charge of the late John Golding, and Dairy Husbandry under James Mackintosh.

There was now a Scientific Staff numbering ten in all, with seven laboratory assistants, a Librarian and a small secretarial staff. The Scientific Staff was soon increased by the appointment of a Head of the new experimental dairy, and the creation of a small Department of Physiology.

A Scheme of Development

The Institute was now able to begin the work of extending and developing its programme in accordance with a scheme already worked out by the Professional Committee and approved by the Board.

It is not possible here to give an account of that development, which can properly be regarded as the beginning of a stage in the progress of the Institute outside the scope of an article on its early history. The following extract from a report on the scheme, prepared in 1920, may however be of interest. It indicates the nature and objectives of the scheme, and also shows how the early pioneering work had led the staff to a realization of the problems calling for investigation.

> "The future work of the Institute should be designed to meet the needs of the Milk and Dairy Industries. These needs are primarily research and advice to enable products of the highest quality to be produced under conditions which give rise to the least wastage and are consistent with economical and efficient production.
>
> The carrying out of this scheme requires that the Institute shall have as complete a knowledge as possible of :—
>
> I. The chemical constitution and other properties of milk and milk products, including their food values.
> II. The different conditions of management of cows and their effects on the composition and properties of milk and dairy products.
> III. The chemical constitution, feeding value and other properties of foods given to cows and their effects upon milk and dairy products.
> IV. The methods of handling and distribution of milk and their effects on the chemical constitution and other properties of milk.
> V. The methods of manufacture of dairy products and their effects on butter, cheese, etc.
> VI. Methods of cropping, stock management and breeding and their relation to successful dairy farming.
> VII. Such other problems the study of which may seem advisable."

These new developments brought renewed financial anxieties which bore heavily on Stenhouse Williams and his staff. There was a debt of £26,000 on the farm and new buildings. There was very little income beyond the Government grant, and the future of several members of staff was very insecure as a consequence. Stenhouse Williams had therefore to devote much of his time in the next few years to the effort of raising funds, an effort in which he was ably assisted by the late Samuel R. Whitley, who became Treasurer of the Institute. This effort involved him in constant writing and public-speaking, which undoubtedly affected his health. His last act was to fulfil a public engagement in Ireland, in February 1932, though obviously unwell. He was taken ill in the train on his way home and died in University College Hospital within a few hours of the time of arrival of his train at Euston. He was in his 61st year.

For twenty years he had devoted all his mind and energy to the creation and development of the National Institute for Research in Dairying. To begin with, he had to fight prejudice and lack of understanding of his objectives. By the end, he had spread the fame of the Institute far beyond the bounds of Britain, and had won for himself a deserved reputation as a pioneer in the application of science to the milk- and dairy-industries.

It was inevitable that he should not have achieved all that he had hoped to achieve. His vision of an Institute of the size and importance commensurate with the magnitude of the industry it is designed to serve had not yet been realized.

But under the guidance of his successor, the present Director, Professor H. D. Kay, the Institute has grown in capacity and in reputation. New buildings have been added, departments of Nutrition, Lactational Physiology, Engineering, and Feeding and Metabolism have been created, and the staff has increased in numbers. There are now about fifty graduate scientific workers in the Institute, and about eighty other staff. Much more is still needed. All laboratories are grossly overcrowded, and the staff is still inadequate. But the vision of Stenhouse Williams, which is shared by his successor, may one day come true.

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IS THERE A DECLINE OF INTELLIGENCE IN BRITAIN?

A Review of Sir Cyril Burt's *Intelligence and Fertility*

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In this pamphlet[1], originally prepared for the Royal Commission now enquiring into the trend of population in Britain, the distinguished psychologist, Sir Cyril Burt, discusses his reasons for believing that the average level of intelligence in the country is declining. It is an observed fact that the average intelligence-test scores of children from large families are lower than those of the members of small families. If test-results are measures of inherited mental capacity, it follows that the less-intelligent sections of the parental generation are reproducing more abundantly than the better endowed, and the population must be steadily deteriorating in intellectual quality. On the basis of the observed mean family-sizes of London children at different grades of intelligence, Sir Cyril calculates the fall as about 1·9 points in the mean intelligence quotient (I.Q.) per generation. If such a fall were to continue, he estimates that in little over fifty years the number of children of high ability (I.Q. of more than 130) would be halved, and the number of feeble-minded children doubled.

Unlike many of his sensation-mongering self-appointed popularizers, Sir Cyril clearly recognizes that this conclusion, based on extrapolations into the past and future from a series of tests all made at the one time, is far from being firmly established. The direct evidence at his disposal—test-results in the same area at different times—is not very reliable. So far as it goes, it indicates that the magnitude of the decline is much exaggerated by his indirect calculations. He also points out that

> " an educational psychologist, familiar with the watchfulness of teachers, would expect that, if a decline of this size had been going on for at least a generation, many of the older head-teachers and officials would assuredly have noticed some of the incidental effects—a decrease in scholarship ability or an increase in the dull and mentally defective."

He therefore urges suspension of final judgement pending the results of a properly-planned large-scale enquiry.

I have carefully worked through the arguments and calculations advanced by Sir Cyril Burt, Professor Godfrey Thomson, Dr. R. B. Cattell and others, purporting to show that national intelligence is declining, and in my opinion they have no case. Indeed, there is some evidence, too weak however to amount to a proof, suggesting that the average mental ability of the population is rising. Underlying all these computations is the basic assumption that intelligence-test scores are completely determined by heredity, so that one can infer the average intelligence of a group of parents from the test-scores of their children. It is indeed true that Burt, Thomson and some of the others agree verbally that test-scores are also influenced by environment, but this admission does not enter into their arithmetic. Yet my detailed calculations show that environmental factors, even on the most conservative estimate of their importance, are sufficiently powerful to account for all the disparities in test-scores that constitute the evidence for the alleged decline in intelligence. I will return to this question later. Meanwhile, I propose to make the point that, even on the assumption that heredity is all-powerful, the computations of Sir Cyril Burt and the others still contain serious fallacies all tending to magnify greatly the size of the apparent decline.

In the first place, the methods used for calculating family-sizes at different degrees of intelligence are obviously incorrect. Burt's figures for average number in the family range from 2·3 for scholarship children to 4·7 for the feeble-minded. It is easy to demonstrate that these figures imply a reproduction-rate of well above unity, whereas it is notorious that the population is failing to maintain itself. It is fairly clear that Burt must have used the biassed method of calculating family-sizes that was exposed by Yule and Greenwood in 1914. When this source of error is corrected, the apparent decline in intelligence shrinks by nearly half.

Secondly, Burt postulates that the average size of family increases steadily with declining intelligence of the parents. This is contrary to all the evidence. All the investigations I have been able to trace, both in Britain and America, agree that the maximum of fertility is reached when one parent is on the borderline of deficiency, parents of lower intelligence than this showing a steady fall in the number of children. Burt's estimate of how far we are breeding preferentially from the least intelligent is therefore much exaggerated.

This conclusion is greatly reinforced by a consideration of the third source of error in Burt's calculations. His method of computation necessarily takes into account only those adults who have one or more children. Sir Cyril is of course aware of this, and notes that allowance should be made for childless adults. He takes it for granted, however, that childlessness is most common at the higher intelligence-levels, so that this allowance would increase the magnitude of the apparent decline. It is true, of course, that the late marriages of professional men, and the marriage-bar on female teachers and civil servants, favoured childlessness among people of high ability. But on the other hand, there is almost certainly a much higher incidence of infertility at the lowest intellectual levels. Only a very small proportion of imbeciles, and virtually no idiots, ever have children. In his thorough ascertainment of mental defectives for a Government committee, Dr. E. O. Lewis found that nearly half the adult defectives were in institutions, where they would be prevented from breeding. Of those living at home, a large proportion of the men are unable either to attract a wife or support a family. Some defective women achieve notoriety by repeated illegitimate pregnancies, but they form only a small proportion of the total, and are far outnumbered by those who never reproduce. I am inclined to believe that childlessness among adults of low mental grade more than counterbalances that among the professional classes, so

[1] [For particulars see *Book Reviews*.]

that the net effect is an increase rather than a decline in the quality of successive generations.

Fourthly, Burt and the others commit the biological error of ignoring the genetic failures. When a graded character is determined solely by heredity, the parents will have the same average genetic composition as that of all the fertilized ova they produce. The new individuals may be aborted or still-born, they may die in childhood, they may reach reproductive age but remain childless, or they may reproduce. It is only this last group that Burt takes into account. Now human miscarriages amount to at least one-sixth of all pregnancies, and there are very cogent biological reasons, as well as much indirect and some direct evidence, for believing that a genetic constitution making for very low intelligence is also likely to favour abortion or early death. It requires only a very moderate incidence of potential mental deficiency among the abortions, stillbirths and early deaths to give a rise of average intelligence in each generation that will more than cancel the decline postulated by Burt and the others. I believe that a process of natural selection against low intelligence has probably been taking place in the human species since its inception, resulting in a slow rise in the average capacity of the survivors. This is naturally a very difficult thing to prove. But it is certainly completely unsound biologically to equate the average intelligence of a parental group with that of the fraction of their progeny who manage to survive the hazards of foetal life, birth, infancy and childhood.

My fifth criticism refers to another instance in which there is a discrepancy between the verbally-acknowledged facts and the assumptions built into the arithmetic. In calculating the alleged decline in intelligence, Sir Cyril assumes that all the parents of mentally-defective children were themselves defectives, while all parents of scholarship children were of scholarship ability. This is of course in flagrant contradiction to all experience. Indeed, Burt himself, in his book on *The subnormal mind*, reports an investigation on a group of mentally-defective London schoolchildren, where only 3 % of the parents were found to be defective. Other investigators get figures of about 15 %. When allowance is made for this error, a notable reduction occurs in the increase in mental defectives and in the decrease in persons of high ability to be expected in future generations.

When all these sources of exaggeration are allowed for, the alleged decline in intelligence shrinks from nearly 2 points of I.Q. to a much more modest figure, probably nearer to ½ than to 1 point. Nor can this difference be accepted at its face value. For, as Sir Cyril states in a footnote :

> " . . . there is a further reason why it may be rather rash to deduce the relative intelligence of the parents from that of the children tested. There would seem to be a negative correlation between intelligence and order of birth. With my own cases it amounts to only – 0.12 . . . Since we are testing fairly young children, it would follow that, whenever we are dealing with members of a large family, we must usually be testing those who are late in order of birth; and . . . these will be the duller representatives of the family."

Sir Cyril does not state which of several possible methods he used in arriving at his correlation coefficient. But if he adopted the most probable procedure, one can calculate the correction to be applied to the apparent fall in intelligence because of the birth-rank effect. It turns out to be at least 0.6 points of I.Q., quite enough to cancel completely the corrected apparent difference between parents and children. In other words, even granting the assumption that only heredity matters, the numerical data presented by Burt indicate no decline whatsoever in the average inborn mental quality of successive generations.

The birth-rank effect does more, however, than dispose of the residue of the apparent degeneration of the population. It challenges the whole set of assumptions on which the calculations are based. If a sixth or seventh child is on the average less intelligent than a first or second child, that cannot be due to genetic constitution. The difference must be environmental, a consequence of such things as less favourable conditions in an ageing uterus, worse nutrition in a family impoverished by more mouths to share the parental income, and the cultural and psychological disadvantages of being at the tail of a large family. Now the material and cultural environment of the older and younger children within the same home is relatively uniform compared with the contrasts between conditions in different homes at varying economic and social levels. If these relatively small differences within the same sibship can produce appreciable effects on intelligence-test scores, how much greater must be the influence of environmental differences within the wide range of conditions found at the extremes of our modern variegated society. Is it not possible that the differences between the average I.Q. of children at different social levels, and in families of different sizes, may be largely, or perhaps completely, accounted for by environment, without invoking any systematic hereditary stratification in average mental endowment ?

One simple way of testing this possibility is to compare the observed differences of I.Q. at different social levels with those known to be produced by corresponding differences in environment. Burt gives a table showing that children of higher-professional men, at one end of the social scale, have an average I.Q. that is about 31 points higher than that of the children of casual workers, while there is a mean difference of about 16 points between children in the lower-professional and the semi-skilled grades. In a well-known study on identical twins, Newman, Freeman & Holzinger describe four pairs who had been reared apart since infancy in homes of different social levels corresponding roughly to the range between lower professional and semi-skilled. Any differences in I.Q. within the pairs must be ascribed to environment. In each case the twin with the better opportunities had a higher I.Q., the differences being 15, 17, 19 and 24 points, giving an average of about 19 points. In other pairs of twins where the disparities between the foster-homes were less marked, the differences in I.Q. were correspondingly smaller, but always in favour of the more fortunate twin. These twin studies are one piece of evidence among many that observed differences in I.Q. associated with social and economic status can be completely accounted for by effects of environment.

There is another way of approaching the question. Sir Cyril agrees that environment has some influence, but he regards it as of less importance than heredity. He quotes with approval the conclusion of Burks, that the contribution of heredity to the total variance in I.Q. is probably not far from 75 % or 80 %, which allows environment to claim about one-quarter of the variance. Although it is easy to show that the contribution of environment is underestimated, let us accept this figure, and ask, " What percentage of the total variance in intelligence is required to account for the difference in the average at different social levels ? " Sir Cyril supplies the answer. He reports that the correlation between children's intelligence and social status amounts to

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INTELLIGENCE AND THE BIRTHRATE

A Reply to Dr. Woolf's Criticisms

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I am most grateful to the editor of the *British Medical Bulletin* for inviting me to reply to the interesting criticisms raised by Dr. B. Woolf. To deal in full with each of the five arguments advanced would need five long and technical discussions; and even these would be somewhat inconclusive, since the writer reveals only the results of his calculations, not the calculations themselves, or the methods on which they were based. However, somewhat similar contentions have been urged in the past by earlier writers, particularly in the USA, and have been discussed pretty fully in the literature. More recently Dr. Blackburn has criticized my pamphlet on much the same grounds; and both his arguments and my replies will be found in a forthcoming number of *Population Studies*.

May I begin by removing a few preliminary misconceptions? First of all, the general trend of the review may give an entirely misleading notion of my own conclusions to those who have read neither the pamphlet itself nor my previous publications. In my pamphlet, as was emphatically stated in the introductory summary and repeated once more in the concluding section, my chief aim was not to prove an alleged decline in national intelligence, but to plead for "systematically planned inquiries" into the whole problem. My reason was that "at almost every stage of the discussion the argument has been gravely hampered by serious weaknesses in the data". If, therefore, Dr. Woolf is seeking to show that there is no conclusive proof of any actual decline, he is merely reiterating what I myself had stressed.

Secondly, Dr. Woolf declares that "underlying all these computations" (namely, those carried out by Professor Godfrey Thomson, Dr. R. B. Cattell, as well as myself) "is the basic assumption that intelligence-test scores are completely determined by heredity". None of us made any such assumption. Indeed, Prof. Thomson and I went out of our way to disclaim it.

> "Every psychologist", I said, "admits that the I.Q.'s furnished by intelligence tests, particularly when accepted without check or correction, may be influenced by schooling and other environmental differences". Thomson writes: "I do not think that environment explains more than a fraction—at most half—of the negative correlation observed" [between intelligence and family size].

Surely this is very different from assuming that the scores are *completely* determined by heredity. Dr. Woolf goes on to say that, even if we admit "verbally" that test-scores are influenced by environment, "this admission does not enter into [our] arithmetic". On the contrary, it enters both into our arithmetic and into the way in which I, at any rate, always attempted to test and correct the crude test-scores. In particular let me repeat that, in the main investigations to which he refers, the calculations were by no means based automatically on "intelligence-test scores" taken just as they came. Every effort was made to check the scores; and dubious cases were not only re-tested, but examined individually in various ways. As psychologist to the London County Council my work was not merely to survey schools by means of tests, but to decide so far as possible which of the dull, backward, or apparently-defective pupils owed their apparent shortcoming to innate and therefore irremediable defects, and which cases were remediable. In those early days both teachers and school medical officers were highly critical of so new-fangled a device as a psychological test of intelligence; and had my assessments been as faulty as Dr. Woolf supposes, there were plenty of sharp observers waiting to report any erroneous decisions. Moreover, an educational psychologist is concerned, not only with discovering cases of apparent backwardness, but also with attempts at remedial education. If, then, Dr. Woolf believes that our methods of assessing the innate intelligence of the dull or defective pupils are erroneously attributing to innate constitution what is really the effect of environmental handicaps, may I suggest that he join us in our efforts at improving the intellectual efficiency of these pupils, and point out to us where we have overlooked an environmental factor?

INTELLIGENCE AND FERTILITY

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0.32. A correlation of this size would use up only about 10% of the variance, out of the 25% which Burt allows for environment. Once again, the admitted influence of environment is more than sufficient to account for all the social disparities in the average of intelligence. There is no evidence of any genetic difference in mental potentiality at different social levels, and hence no reason to suppose that differential fertility can have any deleterious effect on the national stock.

There is no space here to review the evidence suggesting, though by no means proving, that national intelligence is rising. I hope to present this evidence, as well as the details of the calculations summarized in this review, in a series of papers in a more technical journal.

Sir Cyril Burt's plea for a census of national intelligence naturally has my full support. But a comparison of the mean I.Q. of children in 1947 with that of a pre-war generation will prove nothing. If there has been a fall, the extreme eugenist may ascribe it to heredity; but it might equally well be due to the fragmentary schooling and emotional upset of a generation of children subjected to bombing, evacuation, and absence of fathers on military service and mothers in munition factories.

The specialist will regret that Sir Cyril Burt does not make accessible the raw data on which his calculations are based, and that his references to his own previous publications are not always explicit. But although I regard his conclusions as altogether wrong, I nevertheless strongly commend Sir Cyril's pamphlet to the general reader as a sober contribution to a controversy of great public importance, and an ideal corrective of the dogmatism and sensationalism of so many of the advocates of national regeneration through sterilization of the lower orders.

Teachers and psychologists alike would welcome such assistance.

Thirdly, he declares that my conclusion is "based on extrapolation into the past and future from a series of tests all made at the same time". This again is misleading. The testing has been going on for nearly forty years; and in 1939 I was testing the children of parents who themselves had been examined as schoolchildren in or about the year 1914. Our more-comprehensive surveys were repeated at wide intervals. Dr. Woolf may still maintain that the comparisons are too fragmentary to be conclusive; if so, he shares an opinion which I myself expressed. But he cannot claim that my inferences about "the past" were based solely on "extrapolation". In his final paragraph, Dr. Woolf regrets that I have not "made accessible raw data on which my calculations are based". On the contrary, the "raw data" were carefully preserved, and were readily accessible to research students who desired to make use of them. Unfortunately Dr. Woolf himself has not so far made his own data or calculations accessible. He merely asks us to accept his own personal judgement that they disprove, and indeed reverse, the conclusions reached by most other psychologists who have worked on the problem.

May I now turn to his five main points? They fall into two groups. First, he complains that I did not introduce into my calculations certain corrections to allow for various subsidiary factors which he believes would wholly change the conclusions to be drawn. To these criticisms the general reply is the same. Every one of these factors was mentioned in my pamphlet. Further, as I there stated, I myself estimated the range and size of corrections, and found that they would not appreciably change the figures, and that in practically every instance, if made, would strengthen rather than weaken my case. The effects of such factors have been independently considered by such investigators as Godfrey Thomson and Fraser Roberts; and they too reached the same conclusion. Since, therefore, such corrections are always of very doubtful validity, it seemed far better to keep to the lower figures based on the data as they stood. Moreover, in a brief non-technical pamphlet it would scarcely be possible to digress on every page to explain and discuss the nature of the minor and somewhat speculative changes thus introduced. The second set of criticisms attributes to me "postulates" or "assumptions" which in point of fact I did not make (though they may have been made by earlier writers) and which I expressly disclaimed. But to these we shall come in a moment.

1. Dr. Woolf first points out that my simple method of assessing family-size, by taking figures for the number of children already born at the time of my inquiry, yields a reproduction-rate different from that generally accepted for the period in question. Actually the amount of the divergence (which the reviewer does not specify) is exceedingly small. It is true that, as I myself pointed out, it would be impossible to assume that the final size of each family had already been reached. But on an average the parents of the children with higher I.Q.'s are older than those of children of the same age with lower I.Q.'s, and therefore less likely to increase the size of the family. Hence, any correction for this, or any other "bias" in the estimates of family-size, would augment rather than diminish the effect with which I was concerned. Dr. Woolf roundly declares that, when corrections for "bias" are made, "the apparent decline in intelligence shrinks by nearly one half". But he does not tell us how he arrived at this surprising change.

2. A related source of error is said to consist in the fact that I made no allowance for the childlessness of certain adults. As I pointed out, the unmarried (unless they have illegitimate children), and married couples having no children, are necessarily excluded from such surveys. But I argued that these childless adults are likely to be far more numerous among the more-intellectual adults than among the less (consider, for example, the large number of unmarried female teachers). Dr. Woolf, however, considers that we have overlooked the fact that "only a very small proportion of imbeciles and virtually no idiots ever have children". He therefore is "inclined to believe" that the childlessness of the adults in these low mental grades would more than counterbalance that in the higher social classes; and infers that "the net effect would be an increase rather than a decline in the quality of successive generations". But the proportion of adults of imbecile- or idiot-level is less than 1 per thousand. Hence I fail to see how calculations based on actual figures could possibly support the reviewer's "belief".

3. Next, he says, "Burt postulates that the average size of family increases steadily with the declining intelligence of the parents". This postulate, he continues, is contrary to the established fact that parents below the borderline for mental deficiency show "a *fall* in the number of children". But I made no such "postulate". My statement was that, *on the data obtained*, the regression, "except where the lowest defectives are concerned, appears steady and linear". The figures to which he refers, showing a slightly irregular increase in average size of family, were not postulated figures, but observed averages. A more-detailed discussion of the evidence for the linearity of the regressions will be found in Dr. Fraser Roberts' analysis of the data obtained in the Bath survey—an investigation to which, curiously enough, the reviewer nowhere refers.

4. Dr. Woolf also "believes" that a genetic constitution making for very low intelligence is likely to favour abortion or early death. He admits that this would be "a very difficult thing to prove". There are, however, data relevant to the problem he thus raises; and it is hard to see how they could support the somewhat sweeping conclusion he draws. His main contention is that, in view of this alleged correlation, it is

> "completely unsound to equate the average intelligence of a parental group with that of the fraction of their progeny who manage to survive the hazards of foetal life, birth, infancy and childhood".

The effects of differential mortality I have discussed elsewhere. But here the relevant reply is that I did not "equate the intelligence of a parental group with that of the surviving progeny". Admittedly, in previous inquiries, as I myself remarked, "most investigators have sought to deduce the average intelligence of the parental generation from the data obtained from the child generation"; and I added that such a procedure might easily evoke criticisms, like those now advanced by Dr. Woolf. Accordingly, my own procedure sought to avoid such objections by contrasting, not the level of the "parental group" with that of the children, but "the actual level and the possible level of the same generation". To estimate the effect of the differential fertility, therefore, I compared, not the "average intelligence of the parental group" with that of their children, but the average actually attained by the children with the average that would have been attained had fertility been the same in every family.

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5. Dr. Woolf states that :

> " In calculating the alleged decline in intelligence, Sir Cyril assumes that all the parents of mentally-defective children were themselves defectives, while all parents of scholarship children were of scholarship ability."

To begin with, as I have just observed, in the calculations to which Dr. Woolf refers, I myself made no assumption or inferences about the ability of the parents. But even those who did attempt to compare the two successive generations cannot be accused of the assumption which the reviewer suggests. He seems to imagine that, if in calculating a weighted average for a total population from the averages of its sub-classes the computer takes the average I.Q. of a given sub-class to be (say) 120, he thereby implies that *all* the members in that class have an I.Q. of precisely 120. Dr. Woolf goes on to quote my brief footnote on the correlation between intelligence and order of birth. He argues that this correlation would be " . . . quite enough to cancel completely the corrected apparent difference between parents and children." I cannot agree : it would be far too small. But once again to avoid this very type of criticism, I preferred (as I said in the footnote quoted) *not* to base my argument on an alleged " difference between parents and children ".[1]

In his concluding paragraphs, Dr. Woolf suggests that

> " . . . the differences between the average I.Q. of children at different social levels . . . may be largely, or perhaps completely, accounted for by environment . . ."

This is really a side-issue ; but it is one that is frequently raised. Apparently he believes that, if we could only relieve the children coming from the lower social levels of their environmental handicaps, then these lowest levels would provide children with the same high average as is obtained from children of the professional classes. May I therefore ask him to accept this offer ? Let him come with me to one of our better residential Homes, where children are received from their mothers very shortly after birth. Here an occasional boy or girl (usually the illegitimate child of a highly-intelligent father) may win a junior county scholarship, and even (in very rare cases) proceed to a University and obtain a first-class honours degree. If the poor I.Q.'s of the remainder can be " completely accounted for by environment," will he tell us how we can so improve the school and other environmental conditions that every child should do as well as these rare exceptional cases ? Every teacher working in these handicapped areas would be only too grateful to the reviewer if he would tell them how to do it.

Finally, if the low intelligence discovered by the psychologist is due entirely to environmental handicaps, how is it that, when a strain of mental deficiency runs through the ancestry, children from better social levels, living in the most favourable types of environment, still not infrequently show low I.Q.'s ?

In support of this contention, Dr. Woolf refers to one of the many studies on identical twins—a study which Dr. Blackburn has also cited in his own paper elsewhere. Properly interpreted, the data do not in the least bear out his inference ; but it would take too much space to discuss this line of argument here, and for a fuller examination of the matter I may perhaps refer to my reply to Dr. Blackburn.

Dr. Woolf ends this section by arguing that :

> " There is no evidence of any genetic difference in mental potentiality at different social levels, and hence no reason to suppose that differential fertility can have any deleterious effect on the national stock."

That would suggest to the ordinary reader that my argument (like that of some earlier writers before the days of psychological surveys) was based exclusively on alleged differences in intelligence between various social classes. But in my pamphlet I went out of my way to emphasize that the differences to which I primarily referred were not differences *between* social classes, but differences *within* social classes.

He concludes his paper by saying that the plea for a census of national intelligence has his full support. But he adds that, even if such a census shows a decline in the mean I.Q. as compared with that of the pre-war generation, then

> " it might equally well be due to the fragmentary schooling and emotional upset of a generation of children subjected to bombing, evacuation . . ."

There have been plenty of investigations on the effects of bombing, evacuation, etc. There seems no question that it has certainly reduced the school-attainments of children who suffered in that way, but there is no evidence whatever to show that it has affected intelligence when properly tested and assessed. If, therefore, Dr. Woolf has really carried out investigations of his own which contradict this conclusion, he has omitted to quote them. But I rather suspect that this is one of those gratuitous guesses, so often made by " armchair critics " who have not themselves carried out any first-hand fieldwork of their own, and find it easy to forget investigations made by numerous other research-workers when they run counter to their preconceived opinions. Accordingly, until Dr. Woolf is able to give us, not merely a statement of what he personally is " inclined to believe ", but also the details of the calculations to which he refers, it is scarcely possible to assess the precise importance of the objections he has raised. None of the investigators whose conclusions he wishes to reverse would deny that the difficulties he mentions undoubtedly exist. Indeed, they have been the first to draw attention to them. And I myself should hold that the main issues will have to be decided, not by criticism and counter-criticism, but (as I urged in my pamphlet) by more carefully-planned inquiries.

* * *

[1] Dr. Fraser Roberts has dealt with this point more fully in his article on " Birth order, maternal age, and intelligence " in the *British Journal of Psychology (Statistical Section)*, 1947, 1, 35-51.

The sudden death of Sir Joseph Barcroft on 21 March 1947 occurred shortly after the publication of the first volume of his Researches in prenatal life. *Dr. A. St. G. Huggett, who is professor of physiology at St. Mary's Hospital Medical School, London University, has for many years been interested in prenatal physiology, and in the article below he reviews Barcroft's last publication and pays tribute to his influence on its subject*

FUNCTIONAL EMBRYOLOGY

Its Position and its Debt to Joseph Barcroft

Prof. A. St. G. HUGGETT

The problem of life before birth has always had a fascination for the human race, a fascination based partly on the mystical teachings of the great religions in which a non-biological hereditary tree has often been cited as their origin : an interest only paralleled by that of the post-mortem future. In both cases revelation has been rivalled by speculation as the source of information. In view of this, a very considerable amount of belief has centred in all ages upon inadequate factual data. Once again it is to Harvey that we owe the beginnings of our accurate knowledge.[1] His unrivalled capacity for accurate observation, coupled with the experimental approach, laid the foundations of the modern biological approach.

The chain of workers in this field from Harvey to Zuntz (1877) was often broken. The great burst of anatomical work in the nineteenth century led to the development of embryology, but almost entirely as a morphological science, in which functional inferences were made from the histological and anatomical configurations. It was however essential—understandably so—that topography should precede physiology. The names of His, von Spee, Turner, Minot, Hubrecht, Assheton, Hill and Jenkinson form the foundation of our knowledge of comparative embryological anatomy : they are continued in this century by Grosser and Mossman. The story took a big leap forward with the work of Zuntz and Preyer in 1877 who introduced caesarean section upon animals as a method of investigating function in the living mammalian foetus. Curiously enough, this was not adopted as an experimental procedure until 1923. The intervening years included experimental observations of Marshall on the reproductive cycle, and those on the developing egg associated very largely with the impulse given by Jacques Loeb and, later, with the classical experiments of Cunningham on the differential permeability of the foetal membranes. Parallel with this were the early histocnemical observations of Hoffman, Goldman and Wislocki, which contributed much to our knowledge of the absorptive function of the trophoblast.

In 1923-27 the introduction at St. Thomas's Hospital of the technique of caesarean section in a saline bath at 37°C. enabled prolonged observations to be made on foetal and placental function under conditions of experimental leisure, and approximating to the condition *in utero*. In 1932 it was adopted by Barcroft and enabled his energy and drive to create the school of functional embryologists whose results over fifteen years are given in his *Researches in prenatal life*.[2]

Professor J. N. Langley, F.R.S., had died in 1926, at a ripe age while in office as Professor of Physiology at Cambridge. Barcroft was the first holder appointed under the rule of retirement at 65 years of age. On his retirement in 1937 he demonstrated that while a retiring age from active office might be desirable as a general rule, there were exceptions, and that he himself would illustrate this. When in his Chair, his immediate senior lecturer was Adrian. Each pursued his own researches, enlarging the body of knowledge in his respective field. In 1937 Adrian succeeded Barcroft in the Chair and the happy (but rare) symbiosis previously established was continued, and Barcroft pursued his work on foetal physiology in the same building in which he had worked all his life. The energy and drive possessed by Sir Joseph enabled him to build up, between 1932 and his death, a team of workers of ever-changing composition, but all united in enlarging and re-interpreting the body of knowledge on the placenta and foetus. The results are presented in this volume, which was to have been followed by at least one other, which Barcroft's sudden death on 21 March 1947 has prevented from ever being written.

Barcroft aimed at tracing the development of function in the mammalian foetus, as exemplified in the work of himself and his collaborators. The field covered includes certain basic anatomical considerations on the placenta and foetus, many of which have been brought to light by his colleague Donald Barron, now of Yale, and to whom he dedicated the book. Following this, he has collated the papers upon foetal growth and some dietetic considerations governing it, foetal blood-volume and placental blood-flow, the circulation in the chest and through the foetal heart, transfusion of gases across the placenta and their carriage in the foetal blood, and the nervous control of respiration, particularly at birth and immediately after. Eight appendices treat of certain ancillary aspects in which Barcroft frankly relied on the knowledge and experience of others.

There can be no question that the book forms a landmark in experimental physiology, a fitting successor to Preyer's volume on the physiology of the embryo in the last century. Previous to Barcroft's incursion into this field there had been relatively few experimental studies, and no systematic series. Our knowledge was based on histology, morphological embryology, clinical experiences and comparative anatomy and biochemistry. From 1932 to the moment of his death, Barcroft's experiments were designed as a sequence and a co-ordinated whole leading logically step by step to a body of tested knowledge. As a result of the work of Barcroft's team we have had to recast our views upon gaseous transfusion in the placenta, the mechanism of foetal carriage of oxygen in the blood, the mixing of blood in the heart, the role of the foetal nervous system and the existence of fructose in the blood. Most of all, we must approach all foetal

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[1] [For a recent assessment of Harvey's *Exercitationes de generatione animalium* see H. P. Bayon (1947) *J. Hist. Med.* 2, 51.—ED.]

[2] [For particulars see *Book Reviews*.]

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THE EMBRYOLOGY OF BEHAVIOUR

Prof. F. C. BARTLETT

Psychological Laboratory, Cambridge

All over the world, students of human behaviour are happy to acknowledge their great debt to Arnold Gesell and his collaborators in the Yale Clinic of Child Development for their original, elegant and penetrative studies in the early development of individual human conduct. As I begin to write this review of his new work on *The embryology of behaviour*[1], I have vividly in mind a recent visit to Yale. I recall with gratitude the courtesy with which I was met by Dr. Gesell, the beauty of the equipment and methods which he showed me, the intense scientific interest, whether for theory or practice, of many of his records, and the patience and insight with which he met the numerous questions of a deeply-attracted but certainly unspecialized enquirer after knowledge.

In my opinion this is one of his very best books, and that is to say a lot. In it he deals with those complicated and fundamental structures and functions of the human embryo upon which the whole behaviour of man as an individual organism with an independent existence is based. As one reads the story, unrolled here with remarkable economy and clarity of expression, one comes to realize more forcibly than would be possible in any other way, that there can be no real understanding of any form of human skill, bodily or mental, apart from a knowledge of these very early developments.

The book has one outstanding character which distinguishes it from other major contributions to the same topic.

> "We simply assume that as the soma takes shape," writes Gesell, "the psyche likewise takes shape. We are dealing with a single developmental morphology. The infant comes by his 'mind' in the same way that he comes by his body . . ."

It is the sustained attempt to show how everything which in later life comes to be regarded as volitional action has its basic preparation and gains much of its character from the first forty weeks of maturation, that gives the volume its appeal far beyond merely specialist circles. It is not that the highly-trained physiologist and anatomist are likely to find the account of small service. There is in fact no other published work in which the vast detail of experimentally-attested facts about prenatal human development are so comprehensively and at the same time so sparingly recorded. But every intelligent general student of medicine or of psychology, or, indeed, everybody who is intelligently interested in human conduct and its problems, can read it with understanding and great profit.

As already indicated the discussion draws freely upon an immense amount of specialized research. In particular, the outstanding cinema-studies of Davenport Hooker are very fully utilized both in description and in illustration. Also the related foetal studies of simpler organisms carried out by Gonzalez, Barcroft, Kuo, Carmichael, Coronios and especially Coghill are drawn upon.

Here, through picture and through word, we can follow the development, morphological and functional, of supine, prone, sleep-, facial, eye-and-hand and hand-and-foot behaviour of the foetal and the neonatal infant. We watch the emergence, disappearance, re-emergence and final establishment of the basic attitudinal reflexes, and see the specific patterns of interpretation and of movement growing out of them, with fluid and adaptive variations even before the exteroceptors are able to play their increasingly dominant roles. We see all the specialized structures being laid down

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[1] [For particulars see *Book Reviews*.]

FUNCTIONAL EMBRYOLOGY

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placental problems in a new frame of mind. The importance of this book is that in one volume all the evidence of his work is presented as an orderly sequence. Over and above this, it is presented in such a clear and persuasive literary style that the simplest tyro can both follow the argument and observe the logic and the fallacies with ease. It is a pleasure to read, a pleasure enhanced by the work of the publishers.

Barcroft's death marks the end of an era in the physiology of the foetus. If he had lived it would have been extended no doubt, but he himself was moving it on to the next phase. This era extends from the early work of Zuntz to the present date, and can be described as the phase of observational physiology. In this phase has been accomplished for physiology the necessary description of the main processes which occur. Previous to this period, physiological knowledge of the embryo and foetus was largely based on anatomical knowledge and inferences from this. After the introduction of the saline-bath technique in the twenties of this century, physiological facts have accumulated rapidly—largely under the influence of Barcroft's drive, personality, and ability to see the essentials of a problem, to dissect it into its component parts, and to inspire workers in the British Isles, in Europe and in America to tackle the several aspects so exposed. Simultaneously there have been three other lines of approach which are now converging in the new phase setting in. These are: the genetic approach; the endocrinological approach arising out of the study of the oestrus cycle and the development of the fertilized egg; and the obstetric approach arising out of the study of the nutrition of the foetus and the physiology of pregnancy, a study which has itself been fortified by the foetal work of the last twenty years. At the end of this phase we therefore have a fair knowledge of the physiological action of the foetus and placenta.

In the new phase we must look forward to a synthesis of all these lines of approach directed to the study of the peculiarly foetal problems of how function is initiated in the embryo and how it can be controlled. In fact, we may as a result be able to visualize the foetus not merely as a passive individual whose growth or development is outside our control, but as one whose care will be within our power as much as is an adult patient—so far as that is the case. The modern applications of biophysics must come into the field of experiment, to explain how the gene, the hormone, the vitamin, and the nutrient react with the mother to produce the newborn.

Leprosy is a disease which has a fascinating history. In his article below, Sir Harold Scott reviews a new scholarly work by Professor H.-C. de Souza-Araujo on the history of leprosy in Brazil. Sir Harold, after a distinguished career in the Colonial Medical Service, became Director of the Bureau of Hygiene and Tropical Diseases which, among its valuable activities, publishes the Bulletin of Tropical Diseases and the Bulletin of Hygiene. Sir Harold is himself the author of a two-volume History of tropical medicine (1939) *and has an unparalleled knowledge of the literature of so-called tropical diseases in several languages. His review is the product of an exceptional fund of learning and judgement*

LEPROSY IN BRAZIL

SIR H. HAROLD SCOTT

Nearly twenty years ago Professor de Souza-Araujo, of the Oswaldo Cruz Institute, Rio de Janeiro, published his report[1] of a world-tour spent in the study of leprosy in 40 countries during the three years 1924-27. It was, and indeed remains, a work full of interest and replete with information of importance to all leprologists, but readers of it could not help being struck by surprising omissions, for no mention at all was made of the West Indies or of the South American States, countries in which leprosy is rife, and it seemed strange that these should be left out of a world-tour. One of these omissions is now made good by the appearance of the volume before us, the history of leprosy in Brazil.[2] It is a magnificent work and well worth waiting for. The position which the author holds allows him access to original documents and sources of information out of the reach of most, and well has he availed himself of the privilege. In thoroughness and accuracy the work cannot be surpassed, for documents going back hundreds of years have been studied and all the points detailed in this volume are vouched for by *verbatim* quotations from the original sources, of which the authenticity is undoubted and of which many are reproduced in facsimile. The author's self-set task is not yet complete; the present volume, after a brief discussion of leprosy in pre-Colombian times, deals with leprosy in Brazil from 1500 A.D. to 1889; an account of the next sixty years will doubtless be issued later.

Probable Pre-Colombian Freedom from Leprosy

The work opens with a discussion of the highest interest on the origin of leprosy in Brazil; was the disease indigenous or was infection primarily introduced from without? On the one hand we find Chico stating that the Spaniards saw many cases of leprosy when they first went to Mexico in 1519, and that, in his opinion, the disease had been imported from islands of the Sandwich Archipelago with which Mexico had been in touch from ancient times. Cortez, the Conquistador, also is said to have noted that cases were many, and to have actually founded a hospital for their isolation and treatment on the edge of Lake Texcoco, not far from Mexico City. Others have cited the mutilations depicted in old pottery as evidence that leprosy existed and was well known in olden times before there were written records. On the other hand, it is maintained that what has been interpreted as, and called, leprosy was in reality pinta (mal del pinto), now known to be a spirochaetal disease allied to syphilis, and that the facial mutilations depicted in pottery are those characteristic of espundia (a form of cutaneous leishmaniasis) rather than of leprosy.

It is always pleasant for a reviewer to find his theories confirmed by the independent researches of another, hence the gratification of reading that the author comes to the conclusion that leprosy probably did not exist among the aborigines of Brazil. Manoel da Nobrega (1549-60), in his work on diseases of that country, mentions none which could be interpreted as leprosy. Thevet, a Frenchman born in Angoulême in 1502, went to Brazil in 1555, mingled with the native tribes and noted their diseases; though well acquainted with leprosy from his previous travels he makes no reference to any such among the natives of Brazil. Anchieta, it is true, speaks of an individual attacked by a contagious disease resembling leprosy, but this is not worth much, for eleven years later he describes an outbreak of

[1] [De Souza-Araujo, H.-C. *Leprosy. Survey made in fourty countries* (1924-1927) Rio de Janeiro, 1929.]

[2] [For particulars see *Book Reviews*.]

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so that when the time comes it is but a step, across a small threshold, to their effective use. We begin to appreciate, perhaps, more fully the significance of the very early development and perfection of the archaic motor-system, and to understand better the "unconscious" functioning of proprioceptors and interoceptors in later skilled action.

There is of course a thread of theory running through the whole presentation. Out of it all emerges a picture of the essentially anticipatory pattern of human behaviour. Not everybody will agree that the picture is correct, and many details certainly remain to be filled in, not all of which perhaps will be found to fit very well. If ever Sir Joseph Barcroft's latest and most beautiful experiments on human foetal reactions come to publication, some of these details will become available.

Meanwhile the book is one to read, to re-read and to ponder carefully. It matters little whether everything that is said is to be accepted without modification. The story of development that is told decisively and clearly is not only fascinating in itself, but of tremendous importance for anybody who wishes to attain some measure of understanding of the manifold activities of human life.

smallpox in which " the body from head to foot is covered with a leprosy, like vagabond's disease, which might end fatally in three or four days." Anchieta came to Brazil from Teneriffe in 1553, lived among the natives for 44 years till his death in 1597, teaching them and treating the sick. Obviously the condition he described was not leprosy; this disease does not kill in three or four days and, if fatal in the same number of years, the course would be unusually short. If additional evidence is needed, we may cite De Lery and Soares de Souza of the XVI and Coreux, Piso de Liebstad among others of the XVII centuries, who describe yaws and other diseases, but never refer to leprosy as being indigenous; Piso goes even further and states definitely that leprosy was unknown there.

Origins of Leprosy in Brazil

How then did the infection arise, for it became common enough later? Evidence points to two sources—Europe and Africa. First, to immigrants from Europe—Portugal, Spain, France and Holland. The Portuguese brought it to Brazil in 1496; incidentally, it may be mentioned that they were also responsible for its introduction into Madeira, an island free from it until their advent. Next, immigrants from Spain, then from France. Sailors from Normandy and Brittany often voyaged to Brazil and, according to De Lery, many settled there among the natives. There were some 750 leprosaria in France in the XV century, many of them in Brittany and Normandy. Lastly, Holland had many lepers in the XV and XVI centuries, several of them roaming mendicants, and emigration from Europe to Brazil increased greatly in the XVI century.

The european source was, however, a mere trickle compared with the torrent which followed as the slave-traffic from Africa became a thriving industry. Madeira and the Canary Islands were centres whence slaves were transshipped to Portugal and Spain and thence to the west, in particular Brazil. It would appear that to Jorge Lopes Bixorda belongs the odium of having started the slave-traffic to Brazil in 1538. The trade throve apace, and a couple of centuries later a census gave the brazilian population as 3¼ million, of whom a little over 7% were indigenous, 31% were Europeans, and the remaining 62% were Africans, four-fifths of them slaves. Some authors — Juliano Moreira is perhaps the best known — have even gone so far as to say that the Africans were free from the disease until they acquired the infection from the Portuguese and Spaniards after being taken to Brazil. This, however, is protesting too much; all records show that Africa was the " first home " of leprosy —Africa, where today its endemicity is greatest. We may mention incidentally here that the Ebers papyrus (1550 B.C.) speaks of Uchedu or Chon's swellings, and the description of these resembles closely that of leprosy, and the records of Rameses II, two centuries later (1350 B.C.), point to the disease being present among negro slaves brought to Egypt from the Sudan. Brugsch in his *Histoire d'Egypte* (quoted by Hirsch) tells of the prevalence of leprosy in Egypt as long ago as 2400 B.C., in the reign of Husapti.

Founding of Leprosaria

To return to Brazil: the greatest incidence occurred at ports where the slaves were disembarked and introduced into the country, and the districts in Africa whence they were obtained for transshipment abroad were those in which the endemicity was highest. By the first half of the XVII century the prevalence was such as to cause alarm and Martim da Sá, Governor of Rio de Janeiro 1623-32, was the first to take up the question of a leper hospital. Varnhagen in his *History of Brazil* says that such an establishment was founded in 1637, but Professor de Souza-Araujo points out that this is erroneous and that 1637 was probably the date when the people appealed for control of the many lepers who were wandering about the towns unmolested. There may have been a " leper camp " in Salvador, Rio de Janeiro, about this time, the belief being based on legend to account for the existence of the Chapel of San Lázaro there. There has been considerable doubt regarding the first founding of a leprosarium in Brazil. People would complain and send memoranda to the Governors (the correspondence is reproduced in facsimile and one cannot help being impressed with the beautiful and clear calligraphy of those days, an outstanding lesson to modern writers, though the signatures are often partly obliterated by flourishes and ornamentation), who time after time postponed the issue by masterly inactivity, until in 1739 came a final demand for action based on the plea that there were " more than 400 infective lepers " in the town and that a site outside the town should be set aside for housing them. Instructions were given for the matter to be taken in hand without delay and thus came into existence the hospital at São Christovão.

In 1741, a Royal Commission sitting at Lisbon ruled that, as leprosy was contagious, all cases of the disease must be isolated, regardless of class and, with this end in view, they recommended the establishing of lazarettos with separate divisions for the sexes and for the different social classes, and compulsory notification (confidential for the well-to-do) giving the Medical Officers of Health authority over lepers, at the same time warning them of the possible confusion between leprosy and syphilis and of the need for careful examination of imported negroes.

On 31 January 1765, the Jesuit seminary of São Christovão was legally assigned for a leper hospital; the author reproduces a *verbatim* copy of the letter, or deed. At the time of its opening it could accommodate 100 patients, with separate sections for men and women and a central chapel. The place seemed almost ideal. It was by the sea, at an elevation exposing it to breezes from any direction, with a river of sweet water, a large space of level ground for agriculture, and pasturage for milch-cows. Accommodation was provided for the surgeon and his staff, for nurses, for slaves; a residence for the chaplain, a kitchen and a laundry. A copy of the statutes is reproduced defining the general discipline and the duties of the medical staff, nurses, accountants, etc. In January 1766 the patients of the Bobadella asylum were transferred to the new hospital.

Here let us leave Rio for the time and see what had been done in other Provinces of Brazil. *Pará.*—The first reference to be found of the existence of leprosy in the Lower Amazon is contemporaneous with its colonization by the Portuguese and the growth of slave importation. By 1804 it was becoming a social menace and request was made for erection of a hospital to house lepers. In 1816 one was founded in Belém. Vianna, writing nearly a century later, describes it as unhygienic and having none of the security and comfort which an establishment for housing infective persons should have. It was not walled, was not even hidden, but exposed, with many exits for the inmates; males and females lived together

" with the inevitable results." In *Pernambuco* the story is similar ; extension of infection with slave introduction in the XVII century, becoming endemo-epidemic in the XVIII. In 1714 a leper asylum was opened in Recife, in the house of Father Antonio Manoel. This was taken over in 1761 for the Ursuline Sisters, and the lepers were transferred to a larger institute. A small establishment was known to exist in *Bahia* in the middle of the XVII century, in Salvador, and writers mention an old-established place for accommodating *morphoea* (an old synonym of leprosy) patients who had come from Africa and were roaming about the towns. In the Lisbon Archives, in the volume referring to Bahia 1757-1807, is a document regarding a leprosy campaign in that Province. It states that in 1757-8 there were countless lepers wandering unrestricted among the healthy in the towns, and the Viceroy was asked to sanction the erection of an asylum for them. When, later, it was proposed to send " scorbutic patients " (this disease went by the name Mal de Loanda), opposition was raised on the plea that the latter might contract leprosy. The hospital was actually opened on 21 August 1787, as is shown by a facsimile reproduction. Dates given by other writers are thus shown to be erroneous. In *São Paulo*, after considerable agitation and correspondence extending over many years regarding the isolation of lepers in various districts, the Hospital dos Lazaros da Chacara do Olaria was inaugurated in 1804, and patients began to be received there in March 1807. A census of lepers in the Province in 1820 recorded 564 among a population of 126,746 in twenty municipalities, or 4 per thousand. The disease would seem to have been endemic in *Minas Geraes* for a long time before an asylum was founded in 1771 in the Caraça Hills. In 1777 the renowned mulatto artist, Antonio Francisco Lisboa, son of the portuguese architect, Manoel Francisco Lisboa, and an african slave, Isabel, was found to be a leper. He was born on 29 August 1730, and was therefore now aged 47. He lived for another 37 years, dying at the age of 84, after suffering the pain, mutilation and loss of fingers and toes characteristic of leprosy of the mixed type. In 1816, a hospital for lepers was founded in Curabá, a town of *Matto Grosso* ; a list of those concerned with its administration is given, and an order permitting certain officials to solicit alms on days of the month on which no Society was ordinarily allowed to beg for aid.

Care of Lepers in Rio de Janeiro in the Nineteenth Century

Returning to Rio de Janeiro. Everything seems to have gone well for many years, but early in the XIX century complaints were coming in, chiefly of the inadequacy of the water-supply, but on other counts also. Thus, part of the hospital grounds had been granted to a private person, Nicolau Vicini, for erection of a mill in 1809 and, three years later, more ground to Francisco Walis for a cloth-factory ; there were also attempts to interfere with the administration. In 1814, of 182 beds 76 were occupied ; of the patients 17 were Europeans, 38 negroes, and 21 half-castes — 40 less than in 1790. In 1816, owing to the need for housing the military, it was decided that the hospital should be taken over for barracks and a new home chosen for the lepers. The Ilha das Enxadas (Inchadas) was selected, but as early as 1818 complaints were made that the site was unsuitable and the water-supply inadequate. It is worthy of note that in this year, 1816, orders had been issued for protection and aid for children of leper parents and for inspection of those boarded out, to guard against abuses.

The author has introduced a particularly interesting list of addenda to Chapters II–V, with copies of important, hitherto unpublished, documents from the Colonial Historical Archives at Lisbon, including the Proceedings of a Medical Conference held at Rio de Janeiro in May 1740, a minutely detailed plan for leprosy prophylaxis, an account of experiments, extending over a period of months, with a new drug from the plant Sipó d'Onça, and a reasoned report of the findings of the Commission upon it. It allayed irritation, and a decoction assisted removal of crusts, but it had no specific effect on the lesions. One item of particular interest is 25 pages of facsimile reproduction of Ravin's Dissertation on Leprosy and Vandelli's Memorial on the disease. The former is of historical value on the views of leprosy in the XVIII century and deals with the causation, symptoms, complications and treatment, with the author's remarks and a general discussion of the subject.

The third decade of the XIX century was noteworthy in the history of leprosy in Brazil. Here we find, in an official document dated 18 April 1822, the first mention of the idea that the infection might be transmitted by insects (mosquitoes).

Complaints became more persistent regarding the unsuitableness of Ilha das Inchadas as a site for the hospital ; the soil was dry, water-supply inadequate, vegetation and milk lacking, so it was decided to transfer the hospital to yet another site, the Convent on the Ilha do Bom Jesus in the Bay of Guanabara, where it remained as the National (or Imperial) Hospital for the next decade or so, but not under happy conditions. Here, too, the water-supply proved very inadequate and unsuitable. It was by no means free from contamination, but was so charged with impurities that " it not only aggravated the terrible infection from which they all suffered (leprosy) but spread other grave diseases, for example, dysenteries refractory to all forms of treatment by medicine, constipation, chronic inflammation of the liver, and, finally, the cruel disease known as calculus, or stone, in the bladder ; diseases which of themselves may be fatal." The administrators complained of difficulties in enforcing discipline, of patients absconding ; inmates complained of ill-treatment and tyranny on the part of those in charge, of starvation, of deprivation of their dues, of diversion of patients' supplies to the Superintendent's family, of the setting of impossible tasks, neglect by the doctors, etc. The Memorial was sent to the Board unsigned, but it led to a surprise-visit and a thorough investigation. However, the verdict was that the patients' complaints were unfounded, and the inmates, when questioned, denied all knowledge of the Memorial. It was finally traced to a few unruly patients who, against all rules, used to break out to obtain alcoholic drinks, and would barter their food and clothing for forbidden articles. A company of veteran soldiers was sent, ostensibly to prevent patients from absconding, and the acts of insubordination promptly ceased. On another occasion, investigation of a complaint of neglect and ill-treatment resulted in dismissal of the surgeon.

By August 1832, the scheme of housing the lepers had run full circle when a final transference was made back to São Christovão. By a decree, the support of lepers by voluntary contribution was replaced by a Government grant for their maintenance. Naturally, the local residents protested against return of the lepers, but too late ; the transfer had already taken place six months before the protest was sent.

Nevertheless the protest was brought up for discussion at a session of the Medical Society of Rio de Janeiro in March 1833. This Society has had a prosperous and honourable career, becoming later by Royal decree the Imperial Academy of Medicine. Its early publications appeared as the *Revista Médica Brasileira* and thereafter under various names, till in 1906 it became the *Boletim da Academia Nacional de Medicina*, a name which it still retains.

The resultant finding at the discussion on the protest was that no danger need be feared from the proximity of the lepers, that in Madeira the leper hospital was almost in the centre of the town, yet no ill effects resulted, whereas in São Christovão the hospital was some distance from the main residential part.

Some Nineteenth Century Ideas on Treatment and Etiology

From 1830 onwards many discussions have taken place at meetings of the Society and papers dealing with the disease in question have been published in their journal. Some of these are given in detail in the volume under review and cannot, therefore, be passed over without notice. One, of much historical interest, is an article by Dr. de Meirelles written in June 1831, at a time when helminthology was in its infancy and the science of bacteriology a babe yet unborn, comparing and contrasting the two forms of elephantiasis, Graecorum and Arabum, and showing how they differed in course and termination. The author goes on to say that there are certain similarities between one or other of these and leprosy, but that to regard the last as a form of elephantiasis is quite wrong; that obscurity has resulted from looking upon all three as varieties of one disease; and that, owing to this confusion, much of the description of leprosy published previously had been "inexact, erroneous, or unintelligible."

Another paper records that a man suffering from leprosy was bitten by a "cobra cascavel" [a rattlesnake, *Crotalus terrificus*] and was completely cured of his disease in 15 days. This led another patient to allow himself deliberately to be bitten on the hand by one of these snakes. His symptoms, which are described, were typical, and death took place in 24 hours. In September 1839, other similar cases were discussed. The use of cashew preparations, an ointment and the resin, for some time a secret remedy in Maranhão, was the subject of another paper. Like most vaunted remedies for leprosy, this, too, failed to come up to expectations. Other forms of treatment which gained temporary prominence were hot baths, especially those of Santa Cruz, Goya Province, and of the River Pirapitinga. In addition to the hydropathic treatment, those with tubercles had local cautery applied with a hot iron. A paper on the method was delivered before the Imperial Academy of Medicine in June 1845, by Dr. J. M. Faivre. It is reproduced *in extenso* in this volume and is an interesting document; it gives the main chemical constituents of the waters, argues the question of benefit reported from their use and concludes that there are no real grounds for belief in their efficacy. Dr. Faivre adds that the thermal waters, by being deprived of oxygen and atmospheric air, may be the cause of the local prevalence of goitre.

Several points of importance are touched upon in the account of the last half-century of the period dealt with in this volume. The leper hospital is now an excellent establishment, with hot and cold baths, a piped drinking-water supply and a steam laundry. In the first decade of this period a plant known as Assacú or Huassacú, *Ura* (or *Hura*) *brasiliensis*, one of the Euphorbiaceae, was gaining reputation in the treatment of this disease and, incidentally, of syphilis. A gummy, resinous substance was obtained by incising the cortex and it was used both internally and externally. Another remedy which has, contrary to the others, held its own was the *Carpotroche brasiliensis*, the brazilian chaulmoogra. Photographs showing well the fruit, leaves and seeds are reproduced. Other papers and discussions held at the Rio de Janeiro Academy of Medicine are, some of them, sufficiently important to merit reference. The use of "Japeganga tea", an infusion of the root of *Quila japeganga*, one of the Liliaceae, had been tried in a desultory fashion for twelve years or so when in 1845 a plea was made for a more thorough testing of it. Dr. Faivre evidently enjoyed a sound reputation, for his paper on the thermal baths and another on morphoea (leprosy), summing up the knowledge of the time, were sent to the Governor. Morphoea was then often confused with syphilis, but was believed to result from "ingurgitation, inflammation and consequent disorganization of the tissues of the skin", or from eating pinhão (the brazilian vomiting-nut) or the flesh of an animal (pig) which had fed on it. But leprosy existed where this plant was not found. In short, there were many "guesses at truth" as regards the etiology, and the conclusion was reached that leprosy was "an affection of an inflammatory nature of the capillaries of the skin", some maintaining that the capillaries involved were those of the blood, others those of the lymphatics—not a very satisfactory conclusion since the nerve-involvement was disregarded. Lastly, there is Dr. Paula Candido's monograph stressing the differences between syphilis and leprosy, discussing the etiology, especially possible dietetic causes, describing stages of the disease, surveying the treatment, and enumerating many vaunted remedies: galvanism, sudorifics, vasoconstrictors, arsenicals, mercurials, blisters, cautery, elixirs, reptilian poisons, and others—illustrating the old dictum that a disease with many treatments has no remedy. Prophylaxis, he says, "consists mainly in avoiding the things which cause the disease"—a safe guide but one not easy to follow at a time when the cause was not known.

* * * *

Much that is worthy of note has had, for lack of space, to be omitted from this review of a remarkable work. There is a brief bibliography of some special books and documents consulted, but many more records and reports had to be studied to enable the author to write this book. The index is full as regards actual page-references, but it would be of much greater value if these were amplified to save the reader searching for perhaps half-a-dozen or more references to find some particular fact.

Every worker in the tropics and, even more, anyone who is interested in the history of tropical medicine, will be grateful to Professor de Souza-Araujo, who is to be heartily congratulated on this achievement. The motto he has chosen at the beginning of his preface, *Feci quod potui, faciant meliora potentes*, is a happy one, but he need fear no rival.

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BACTERIA IN THE KITCHEN

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For good or ill, bacteria have much to do with food. The good they can do, if we include fungi, embraces the fermentations which produce wine, beer and vinegar, and the complex changes which give their distinctive flavour to many kinds of cheese. Their evil propensities are of two kinds—the simple spoiling of food by decomposition, and the production of specific forms of bacterial food-poisoning. How to prevent spoiling was known long before bacteria were recognized as its cause. All methods, whether ancient or modern, convert the food into a medium which will not support bacterial growth, or destroy the bacteria contained in it. Heat is almost the only agency which will achieve the second of these purposes : the first can be attained in many ways. One of these is drying, which has for long been used for meat of many kinds, more recently for milk, and only in the past few years for vegetables and eggs. An alternative is to raise the osmotic pressure to a point incompatible with bacterial growth : this can be achieved by either pickling in brine or by adding a high concentration of sugar as in jam-making. The use of cold is almost too familiar to need mention, but it is worth while to remember that this, too, simply prevents bacterial growth : so far from being lethal to most bacteria, it tends to prolong their life. Finally, chemical preservatives which act as antiseptics may be used : some of these, such as formaldehyde, are harmful, and their use is illegal : others, including boric, salicylic, sulphurous and benzoic acids are relatively harmless when used in limited amounts.

These are some of the matters dealt with by C. E. Dukes in a little textbook entitled *Bacteria in relation to domestic science*.[1] Bacteriology is now one of the subjects taken by students in Domestic Science and Household and Social Science, and this book tells them what they need to know of the general properties and distribution of bacteria, of their beneficent and destructive activities, and finally of specific forms of bacterial food-poisoning. It is written in a pleasing style, technical terms being either avoided or interpreted in simple language, and contains much material of interest to other kinds of reader than the students for whom it is primarily intended.

Food-poisoning from Dried Egg

Dukes mentions duck's eggs as a possible source of *Salmonella* enteritis, but his book has appeared just too early to include a reference to a recent Medical Research Council Report[2] on the transmission of such infections by dried-egg powder. The story told here goes back six years, to the time when it was decided to improve the british national dietary by the large-scale importation of dried egg from America. This was at first issued only to confectioners and caterers, but in July 1942 it was issued to the public. Only one month later, bacteriological examination revealed that some samples contained living organisms of the *Salmonella* group. A courageous decision was then taken about which the public and most of the medical profession knew nothing at the time : this was to continue importation, on the grounds that the benefit in nutrition outweighed the risks involved. Although the risk was proved by subsequent events to be genuine, this difficult decision will receive full approval in retrospect.

The Emergency Public Health Laboratory Service, as well as the Ministry of Food Laboratory, investigated this problem from every point of view during the latter part of the war, and this report contains the results of their work. That dried egg did cause a good deal of *Salmonella* enteritis is proved not only by the study of individual outbreaks, but by a survey of the incidence and bacteriology of the disease throughout the war-period. A rise in the apparent incidence in 1940 was almost certainly due to the establishment of the Emergency Public Health Laboratory Service itself, and the consequently improved facilities for diagnosis. A much more spectacular increase in 1942 signalized the advent of dried egg-powder as an item in the household ration. This merely circumstantial evidence is verified by examination of the species of *Salmonella* concerned : no less than 24 species appeared which had never been known to cause human infection in Britain before. These, of which the commonest were *oranienberg*, *montevideo*, *meleagridis*, *bareilly* and *anatum*, were also those most frequently found in samples of dried egg. These are also for the most part strains which have been found in the faeces of poultry in America. Alternative explanations, improbable as they may seem in view of these facts, are carefully considered. Among other branches of this investigation, a survey was made of the incidence of these infections in pigs in Britain, and many of the same new species were found, none of which had been isolated from pigs in a similar survey made by W. M. Scott shortly before the war. A secondary effect has evidently been to establish these new infections in our pig population.

It is clearly of the utmost practical interest to know in what circumstances these organisms can survive cooking. Scrambled egg, omelette and custard were prepared from samples known to contain Salmonellas, cooking times being carefully regulated and the temperature observed. In no case were the organisms recovered in culture after cooking, nor did they survive admixture with vinegar in preparing salad-dressing. On the other hand, when the egg was first " reconstituted " (i.e. mixed with water or milk) and incubated overnight before cooking, some of the organisms survived and multiplied again in the cooked product on standing. Survival seems therefore to depend chiefly on numbers : there are comparatively few in the dry product, but if they are enabled to multiply before cooking, the chance of survival is much greater. The effect of their multiplication after cooking was clearly illustrated in one outbreak resulting from the consumption of scrambled egg, when some of this food was set aside in warm weather and served again at a subsequent

[1] [For particulars see *Book Reviews*.]

[2] [For particulars see *Book Reviews*.]

meal, the partakers of which were the chief sufferers. The risk in using dried egg can therefore be minimized by preparing only as much of any dish from it as is needed for immediate consumption.

Ice cream

The potential dangers of ice cream have long been recognized, and were emphasized by the outbreak of typhoid fever at Aberystwyth last year caused by a carrier who was an ice-cream vendor. New regulations requiring the pasteurization of the mixture from which ice cream is prepared were made by the Ministry of Health at the end of last year. Those responsible for the supervision of this product will be interested in the new and simplified test for hygienic quality devised by the Public Health Laboratory Service and described in a recent report[3]. There has hitherto been no standard method of examining ice cream bacteriologically, although Compton & Youssef[4] and others have adapted for this purpose the total plate-count and coliform-count as formerly used for milk. The new method is an adaptation of the methylene-blue reduction test, and gives similar information about the extent of bacterial contamination by much simpler means.

The Flora of Food Utensils

Glass- and china-ware, spoons and other utensils in places of public refreshment can obviously act as vehicles of infection. This is of course recognized in hospitals, where the food utensils used by a patient with an infectious disease, whether a streptococcal sore throat, tuberculosis, or syphilis, are not only boiled after use, but kept for the use of that patient only. The examples mentioned were chosen because they are all conditions from which a person may be suffering and nevertheless visit a public restaurant. Many others might be mentioned, including dysentery and Vincent's infection. Anyone can see that the methods used for cleansing glasses and cups in some places of refreshment are quite inadequate and insanitary. This problem has been attacked with vigour in the USA, where mechanical dish-washing and the use of germicidal detergent solutions or high-temperature drying are now fairly common. It has even been accepted that a properly "sanitized" utensil should not yield more than 100 bacteria of any kind on cultivation. Some indication of the progress being made in that country is given by the fact that three papers in a single recent issue of the *American Journal of Public Health* (April 1947) deal with this subject.

It is encouraging to see that Britain has not altogether forgotten this neglected aspect of public hygiene. R. Knox & Jacqueline Walker[5] made a study of the flora of large food-containers used in kitchens, with the idea that these vessels might be implicated in the spread of intestinal infections on a considerable scale in restaurants or factory-canteens. These vessels often contained large numbers of bacteria, and the numbers could be reduced to a harmless level either by steam-sterilization, or by thorough washing with soap or a detergent, wiping with a sterilized cloth, and finally rinsing with very hot water. R. Irene Hutchinson[6] presents much more alarming data, based on the cultivation of swabs from spoons, cups, forks, plates and glasses in use in hotels, restaurants, canteens and other places of refreshment, presumably of an average standard of cleanliness. Pathogenic or potentially-pathogenic bacteria were frequently found: they include various intestinal coliform bacilli, with one example of dysentery bacilli (Sonne type, from a spoon), *Staph. aureus* (coagulase-positive) and haemolytic streptococci (of several Lancefield groups, including one strain of group A from a fork). Samples of dish-washing water were sometimes found to contain as many as 1,000,000 living bacteria per ml., which is the approximate bacterial content of sewage. It is perhaps noteworthy that soap and other cleansing materials, towels and cloths are at present very scarce in England: these shortages may be a factor in rendering present conditions worse than they need be. But it is quite clear that the protection of the public in places of refreshment requires a radical change of method from the primitive rinsing and wiping which is still so common. No department of food-hygiene has been so neglected, and it is at least encouraging to read that the proprietors of the premises visited during this survey were interested, helpful, and "eager to know what measures could be adopted to remedy defects".

[3] *Mon. Bull. Minist. Hlth.* 1947, 6, 60
[4] *J. Hyg., Camb.* 1946, 44, 289
[5] *J. Hyg., Camb.* 1947, 45, 151
[6] *Brit. med. J.* 1947, 1, 134

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CHEMOTHERAPY FOR EVERYMAN

A Comparative Review of Three Recent Popular Books

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The increasing social importance of science—indeed, its now overwhelming importance—has impressed scientists with the urgent need for the results and implications of their work to be interpreted to the public. There is, however, no general agreement about the way in which this interpretation should be effected. At one extreme are those sticklers for precision who demand that works intended for the general public should be written by the scientific specialist, who should confine himself to his own limited branch of science. At the other end of the scale are those who proclaim themselves realists and state that to achieve the necessary wide circulation readability is the supreme need and that even scientific accuracy may to a considerable extent be sacrificed in achieving it. Both manifestly have reason on their side. While far more harm than good will be done by presenting to the public a distorted, inaccurate and incomplete view of science it is equally futile to provide scrupulously correct and polished accounts which are so heavy in style and content as to have a negligible circulation. Between these extremes are such alternatives as co-operation between a professional scientist and an experienced writer—open to all the objection of divided authorship—and the cultivation of science-writing as a profession, those who practise it being required to conform to prescribed scientific and literary standards. For providing the bulk of scientific reading-material to the public the properly-qualified professional science-writer is perhaps the best, if far from ideal, solution, though the scientific specialist who can make an occasional contribution to popular literature and the unqualified writer who will make an occasional excursion into the realm of science both have valuable parts to play.

The writer who attempts to interpret the results of medical research is in rather a difficult position. Although assured in advance of a wide circle of readers—for public interest in the functioning of the body in health and disease is considerable, even if sometimes rather morbid—very great care is needed in the treatment of the subject. On the one hand there is the fact that the full value of the proposed new public medical services, and of the existing ones, will be realized only with the co-operation of a public sufficiently well informed to appreciate the nature of the services available to them. On the other hand much harm may be done and misery caused by giving, accidentally or otherwise, false impressions about new methods of treatment and similar matters. This danger is, of course, particularly great in the case of diseases, such as cancer and tuberculosis, for which existing forms of treatment are unsatisfactory. The false hopes raised and the bitter disillusionment caused by irresponsible writing on medical subjects are lamentable.

Three recent popular scientific books[1], linked by the common theme of chemotherapy, form an interesting example of the different ways in which different kinds of author approach the subject. In *Molecules against microbes*, E. S. Duthie tells the story as a medical man who has first-hand and first-class knowledge of bacteria and the chemical agents available to destroy them within the body. He picks his way with certainty among the technicalities of the subject, and provides a clear answer to almost every question which the general reader might expect the text to deal with. Margaret Goldsmith, in *The road to penicillin*, deals with the subject from an essentially historical and literary point of view, avoiding technicalities, especially in the field of chemistry, with frank determination. The style and arrangement is, except in the last chapters, good and well calculated to arouse and maintain the interest of any intelligent reader. David Masters, in *Miracle drug*, relates the story of the discovery and development of penicillin—providing a certain amount of general discussion of chemotherapy as a necessary background—as seen by a practised journalist who has made a considerable, if not wholly successful, effort to get his facts right by consulting both the scientific literature and the pioneer research-workers concerned. His style is essentially dramatic. The text is punctuated by the frequent superlatives and overstatements which seem to be inseparable from popular journalism. However much this may be deplored by the literary stylist, there is some evidence that the general public likes the journalistic style and may indeed find it, if the emphasis is rightly laid, a valuable aid in picking out the essentials of the subject.

From the technical point of view *Molecules against microbes* is much the best of these three books. It is packed with information logically and clearly displayed according to a well-conceived scheme. The bacteriological and chemical background of the subject is thoroughly dealt with and the discovery, use, and limitations of almost every accepted chemotherapeutic agent are described. The chapter on penicillin is particularly interesting because of Dr. Duthie's own personal association with members of the Oxford research team. So far as the general reader is concerned, the chief criticism that can be made of the book is that it is too thorough, that the author has introduced factual material at the expense of readability. There is, however, no better introduction to chemotherapy available for those prepared to take a little trouble in ascertaining the essentials of the subject. Apart from being of value to the intelligent lay reader, the book should form a good introduction to chemotherapy for the medical student.

The main features of *The road to penicillin* have already been discussed. The historical treatment is excellent and the author has acquired the ability, invaluable to the popular writer, to sustain interest by the frequent introduction of unusual items of information. There is a good deal of verbatim quotation from contemporary writings, indicating considerable historical research. It is in the later chapters, dealing with the last century, that the author ventures on to less-certain ground. Her excursions into the technicalities of chemistry are not always happy ones, and she wisely refrains from making them more frequently than is absolutely

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[1] [For particulars see *Book Reviews*.]

We publish below some impressions by a distinguished representative of chinese medicine, written in the course of a visit as a guest of the British Council. The hope expressed by Dr. Chu, Dean of the National Medical College of Shanghai, for a strengthening of sino-british medical relations will find a particularly strong response among those who have had the opportunity of appreciating the intellectual and personal qualities of chinese colleagues. Dr. Chu's remarks are addressed particularly to british colleagues, but they are doubtless equally applicable to many other countries which have something to give to, and receive from, China

SOME THOUGHTS ON MEDICAL EDUCATION PROMPTED BY A VISIT TO BRITAIN

DR. H. P. CHU

During a period of about three months spent in Britain I visited London, Oxford, Liverpool, Edinburgh, Glasgow and St. Andrews. So hurried was the trip, that any observation I have made will necessarily be superficial and any comment on the medical education would seem premature at this moment. Concerning this subject, there is valuable information in the report of the Inter-departmental Committee on Medical Schools ("Goodenough Report", 1944). Views and opinions expressed there are largely based on the evidence received from a large number of organizations and from individuals who are specially qualified to give helpful information and advice. It gives a comprehensive account of the conditions in various medical schools both before and during the war; it treats exhaustively of undergraduate and postgraduate training in respect of students, equipment, distribution and number of teaching medical centres, etc.; it offers suggestions and recommendations for the improvement of the british method of medical education. Though primarily written for the United Kingdom, in many ways it provides useful guidance also for us in China.

With regard to the teaching of pre-clinical sciences for example, it has pointed out that there is an urgent need in every school for a new viewpoint on the part of teachers of the preclinical subjects, and for the drastic elimination from the curriculum of a mass of detailed information which serves only to clutter up the student's mind and to deaden his interest in subjects that could and should be of the liveliest appeal to him. This may be exemplified by anatomy. The traditional method of teaching this subject is to let the student dissect a human body, and to commit to his memory a vast number of structural details.

Very much to the point is the remark made to me by Professor W. E. Le Gros Clark of Oxford, who said that dissection of the human body could be appreciably reduced, and that in routine teaching of topographical anatomy, form and structure should always be correlated with function.

In the Report some mention was made of social medicine. Its importance and scope is well summarized in the statement of the General Medical Council, which is quoted in the Report as follows: "The Council are of opinion that the study and teaching of Social and Preventive Medicine deserve further encouragement, in order that medical students and practitioners may be better acquainted with the influence of social, occupational, genetic, and domestic factors on the incidence of human disease and disability."

Oxford has an Institute of Social Medicine. Edinburgh and Glasgow place social medicine in the department of Public Health. What position it should occupy in medical

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CHEMOTHERAPY FOR EVERYMAN

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essential. It might indeed be argued that even this minimum is not reached, and that for a book which sets out to give the history of chemotherapy the chemical treatment is far from adequate. Against this, however, it may be said that the general reader's knowledge of chemistry and chemical principles is so meagre that, unless an undue amount of space is given to their explanation, it is largely wasted effort to discuss them in any detail in a book of this kind. The last two chapters, describing the discovery and development of penicillin itself, are disappointing. Having travelled the long road to penicillin from the time of Hippocrates the reader might reasonably expect that particular care would be taken to ensure accuracy and balance in this last lap, but this is not the case. Dr. Chain, for example, than whom no one has done more to advance our knowledge of penicillin and whose services were recognized by a share with Florey and Fleming in a Nobel Prize, is scarcely mentioned. When he is mentioned he is submitted to the indignity of having his name constantly misspelt. Nevertheless this is a book which, taken as a whole, should convey to the general reader a good idea of the history of chemotherapy and the present possibilities and limitations of the method. It is very readable.

Miracle drug deals, as already mentioned, exclusively with penicillin. Although open to criticism from he literary and factual point of view, it is, on the whole, one of the best popular books on penicillin that have yet been published. In particular, it is one of the few that give fair credit to the Oxford team, whose remarkable achievements are not yet fully appreciated even in Britain. All the essentials to an understanding of the discovery, development, manufacture, and use of penicillin will be found in this book. It is, however, embedded in a dense matrix of melodramatic and not always relevant material. Particularly aggravating is the technique—used by many other popular science writers—of putting conversation into the mouths of the principal characters. At this time it is obviously impossible to recall what was said in the course of casual conversation to which no particular significance then attached. Much of the conversation which is included in the book must therefore be purely fictitious, unconvincing, and quite valueless. Like *The road to penicillin*, this book has the important virtue of being readable, but it is likely that those who enjoy the emphatic, dramatic, journalistic treatment of David Masters will not like the much quieter and more scholarly approach of Margaret Goldsmith, and vice versa.

Although these books form a trilogy with chemotherapy as the common theme they cover different ground and approach the subject in so different a way that they are by no means mutually exclusive ; all three can well be read with interest and profit.

curricula, time will tell, but that greater emphasis has been placed on the subject is quite apparent. In China, apart from the high rate of morbidity and mortality due to preventable diseases, there is an untold amount of suffering, misery and disability, which is often of our own creation, and to which we cannot close our eyes. It is only through the teaching and practice of social medicine that we could hope to find a solution of the problem.

The Goodenough Report has called attention to the salaries paid to teachers in pre-clinical and in clinical departments, and suggested that a national range of salaries with a lower and an upper limit be devised for each grade of teachers in the medical schools. We doubt if such provision would provide a complete solution of our problem in China. Time and again we have been disappointed by those who, holding full-time appointments, were loyal and devoted to the post at the time when they first joined the staff but, after a while, when enough contact had been made with patients, began to see patients privately in violation of the hospital rule. When warned for the offence, they simply resign and enter into whole-time practice. In the absence of an effective remedy to deal with such cases, the report is perhaps correct in saying that the vital matter is to appoint persons of the right outlook to the professorships.

So I could go on to dwell on many other points in the Report which are of concern to medical education in Britain as well as in China, but the mere repetition of them would be superfluous. It must suffice to say that it is a very valuable book for our reference.

After all, the standard of the medical profession in Britain is well guaranteed by the General Medical Council, the functions of which are to prevent the unfit from gaining access to the Medical Register and to remove the unworthy from it. In China there exists no such machinery. What we do is to grant a person a licence to practise medicine so long as he is graduated from a medical school that is registered with the government, and in standard there is considerable variation among the different schools. The most effective way of upholding the quality of medical education seems to us to subject all medical graduates, regardless of which schools they studied at, to an examination to be given by the Examination *Yuan*, the National Board of Examination. If this could be carried out, the poor schools would either have to improve or close.

During my stay in Britain, what has specially claimed my attention are the facilities for postgraduate training in medicine. To a chinese student who is looking for an opportunity for advanced study, three alternatives are open: (i) house-appointment, (ii) research fellowship, and (iii) regular postgraduate course.

House-appointments are unlikely to be possible at present, since a large number of army doctors have been released from service, and they must make up time lost during the war.

By making an arrangement sufficiently in advance, one can usually obtain permission to work in a research laboratory where there are good supervision and guidance. There is no need to expect anything too elaborate in the way of equipment. As a matter of fact, of the laboratories which I have visited, very few are elaborately equipped but most are well provided with such auxiliary services as those of a mechanic's shop, glass-blowing and photographic departments, animal-houses, departmental libraries, etc. These are rather vital to a research laboratory. Another point which impresses me is the teamwork in research, there being good co-operation between men of different specialities in a problem of common interest. The discovery of penicillin is a typical instance of the case. Nor does it matter if a student can make a discovery or not. So long as he has acquired the habit of learning by himself, and has learned the methods of approaching and executing a problem scientifically, we should not have to worry about him, because he can develop himself when he returns home.

The postgraduate course is generally very intensive and comprehensive. That in medicine, offered by the Edinburgh Postgraduate Board for Medicine, can act as an example. It lasts eleven weeks, and covers cardiology, respiratory diseases, alimentary diseases, haematology, psychological medicine, paediatrics and biochemistry in clinical medicine. Training of this kind would be valuable for a chinese student, because when he goes home he may be called upon to attend a multiple variety of conditions in internal medicine in places where a specialist's services are not obtainable. In order to get the full benefit of the course, a student, before he comes, should have had an adequate amount of practical experience in a clinical field of medicine. In London there is the British Postgraduate Medical Federation which, apart from offering within its own area courses in general medicine, general surgery, obstetrics, pathology, diseases of children, laryngology and otology, neurology, ophthalmology and psychiatry, acts as a source of information on the postgraduate facilities available in the United Kingdom.

In China, before and during the war, there was a shortage of teachers in both pre-clinical and clinical fields, and the shortage is even greater now because existing schools are expanding and new schools being established. To such agencies as the British Council, Sino-British Cultural Association, ABMAC, the Rockefeller Foundation, etc., we are deeply indebted for the creation of many fellowships which enable chinese medical graduates to carry on advanced study either in Britain or in the USA. Fellowship-winners are those who have passed a competitive examination in technical subjects, as well as in the english language. Fellowships are awarded to the best and most deserving. It is gratifying to know from various sources that the Fellows are doing hard and often admirable work and will be, we believe, the type of teachers required for our purpose. The results would seem to justify the expenditure.

While China is under heavy obligation to friends, american and british, for their assistance in training her medical and health personnel in the stage of rehabilitation, still no small amount of expense is involved in the maintenance of those fellowships. Furthermore, that only takes care of a limited number of those who need further training. Six or seven hundred doctors graduate in China each year. If they are left to their own plight, we are afraid that many of them would virtually degenerate into quackery, which from the educational stand-point is not only wasteful but harmful. What is needed is obviously a provision for postgraduate facilities at home in addition to fellowship-training abroad. At the moment, no ambitious scheme should be attempted, but every possible resource, governmental and private, missionary and non-missionary, should be made available for the purpose. The combination of

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SHERRINGTON'S "THE ENDEAVOUR OF JEAN FERNEL"

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Those who have read Sir Charles Sherrington's fascinating Gifford Lectures, *Man on his nature*, will recall the attractive figure, therein painted with a loving pen, of Jean Fernel, the french physician of the Renaissance, the author of the first printed work on physiology, indeed the first work of its kind since Galen's famous "On the Use of Parts", and the actual coiner of the word "physiology". In his little and most charming work, *The endeavour of Jean Fernel*[1], Sir Charles has returned to what is manifestly a favourite subject with him, has displayed his hero with sympathetic insight, and has created for his readers a vivid picture of the times and the intellectual climate in which Fernel strove to emancipate his thought from the animism which had hitherto so deeply coloured medicine.

Fernel may be said to represent Renaissance medicine shaking off its long association with astrology and magic, and slowly but surely groping its way to a place within the fold of natural philosophy. Yet the full emancipation of medicine had to wait yet another century until Harvey's great discovery, and his classic *De motu cordis*, had dispossessed medicine once and for all of the cardinal qualities, the humours and the temperaments, the elemental and the innate heats and the coctions, and all that animism which must have acted so potently against the unhampered use and development of the method of observation. It was Harvey who set medicine and physiology upon the path they have since trodden so fruitfully. Fernel was but a precursor, but it is against the medicine of Fernel's age that we can see most clearly the magnitude of Harvey's achievement, which opened a gate to a world of biological science that we are still eagerly exploring.

Fernel lived between 1497 and 1558, and his career as a physician occupies approximately the last 30 years of this span. In seeking to trace the evolution of Fernel as a young master of arts in the University of Paris, through the period of his preocupation with mathematics and with astrology, to his final emergence as a physician persuaded that man must be studied as a natural object and medicine as within the natural law, Sir Charles Sherrington has followed Plancy, Fernel's disciple and biographer, and from this and other sources has sought to depict briefly the intellectual background of contemporary life in the University of Paris against which the young Fernel developed.

It is perhaps peculiarly difficult for us in this age to possess a sympathetic insight into the intellectual climate of the Middle Ages, more difficult, indeed, for a scientist than for the historian, and therefore it is not altogether surprising if the distinguished author of this charming appreciation of Fernel tends unwittingly to enhance the merits of his subject by setting him against a somewhat darker background than full justice to the mediaeval world allows. It is not for nothing that the thirteenth has been called "the greatest of centuries," for it was the age in which scholastic philosophy achieved its full development, and the University of Paris was the shrine to which all mediaeval scholars turned. True it is that scholastic philosophy had lost its unity and was already far in decline by the end of the fifteenth century, when Fernel lived, but in dying it had left a rich legacy to the age of the Renaissance—a legacy not yet exhausted.

It is habitual with us in this age of "progress" with its technological wonders, technological barbarisms and barbarians, and its technological potentialities for yet more destruction and human misery, with its collapse of ethical sanctions and its social disintegration, to look somewhat patronisingly upon the Middle Ages, and to dispose of them in our minds as an age of logic-chopping and sterile disputation. Yet a modern philosopher and mathematician has reminded us of what we owe to that eminently rational age, before men had exchanged old lamps for new—a faith in Heaven and the angels for faith in science and the atom

[1] [For particulars see *Book Reviews*.]

THOUGHTS ON MEDICAL EDUCATION

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training both at home and abroad may in the course of time somewhat relieve the shortage of teachers.

Space does not permit me to write too long a story about my visit but before concluding, may I have the privilege to pass an opinion to our british medical colleagues. Though we are separated by distance and by differences in language, way of living, tradition, etc., we are nevertheless bound together by a common task in which you and I are engaged for the advancement of medical knowledge, for the protection and promotion of health and for the betterment of society. While you have already built a solid foundation in scientific medicine, we are only just laying the corner-stone; while you have already had such a number of doctors as would meet your need, we are still in serious shortage of them; while you have already caused many of the infectious diseases to disappear from your country, they still constitute a serious menace to us. So many are our shortcomings that there is much that we shall learn from you and at the same time, we believe, there is also much in us, which would be of interest to you. Shall we not, beginning from today, bring ourselves into closer touch by establishing a channel through which ideas may be exchanged freely between us?

The above few lines represent a portion of my thought on the eve of my departure for home, and they also must serve to express my feeling of deep gratitude to those who have assisted in various ways to make my trip happy and profitable. Indeed there has been extended to me such an overwhelming hospitality that I do not know how I am going to repay it. I shall take home all these pleasant memories.

bomb—with who can guess how little increment in human happiness? In tracing the origins of modern science, Whitehead[3] points out that the Middle Ages formed one long training of the intellect of Western Europe.

> "There may have been some deficiency in respect to practice," he writes, "but the idea never for a moment lost its grip. It was pre-eminently an epoch of orderly thought, rationalist through and through. The very anarchy quickened the sense for coherent system . . . It needs but a sentence to point out how the habit of definite thought was implanted in the European mind by the long dominance of scholastic logic and scholastic divinity. The habit remained after the philosophy had been repudiated, the priceless habit of looking for an exact point and of sticking to it when found. Galileo owes more to Aristotle than appears. He owes him his clear head and his analytic mind. I do not think that I have even yet brought out the greatest contribution of mediaevalism to the formation of the scientific movement. I mean the inexpugnable belief that every detailed occurrence can be correlated with its antecedents in a perfectly definite manner, exemplifying general principles. Without this belief the incredible labours of scientists would be without hope. . . . the faith in the possibility of science, generated antecedently to the development of modern scientific theory, is an unconscious derivative from mediaeval theology."

The foregoing is a lengthy passage to quote in what is no more than a brief appreciation of a biographical study, but it embodies truths so generally unknown to moderns, and so alien to our thought of the Middle Ages, that its full citation asks for no apology. Least of all, then, may scientists scorn the Middle Ages.

It is clear, however, from Plancy's account that the young Fernel had taken his M.A. degree at a time when the new humanist learning had not established itself in the University of Paris, and that Fernel himself was deeply aware of what he had missed, so aware that he turned back for another five years to classical study and to the grammar and rhetoric which, so Sir Charles Sherrington tells us, the new learning took so seriously, and not, as did the mediaevals, as "mere lessons in memorizing maxims for divinity". Yet surely, grammar, rhetoric and logic formed the very foundation of the educational system of the mediaeval university, under the name of the Trivium. Their association was with philosophy and not with divinity or its maxims. They were the keen intellectual instruments of the coldly rational thought of the age. And rhetoric, that much abused term, was not merely "the art of persuading", but the art of the expansion and condensation of discourse by the use of metaphor and analogy. There is no good literature without rhetoric, and we who have in the psalms of the Authorized Version of the english Bible what is perhaps the loveliest and most uplifting rhetoric in any tongue do well to honour rhetoric.

The new learning could not indeed take grammar and rhetoric more seriously than did mediaeval learning at its best, and we can well do honour to Fernel and the Renaissance world in which he grew up without setting them against the synthetic background of a largely fictitious dark age. Indeed, it was perhaps as much from the medicine of the Renaissance as from that of the Middle Ages that Fernel sought to emancipate himself and medicine, and to bring the latter within the fold of natural philosophy.

In his account of this intellectual odyssey, Sir Charles writes with the insight of the scientific genius and humanist that he is, giving an intensely human picture of Fernel as thinker and as practising physician, and showing how the germ of the observational and inductive method grew in his mind so that finally he turned wholly away from his earlier preoccupation with, and belief in, astrology, yet never succeeding in weaning himself from the animism of his day. Within the limits of this review I do not propose to summarize this story, for it is one every serious student of the history of medicine should read and contemplate for himself; but in conclusion it is impossible not to express a delight in the rich bibliographical knowledge displayed so modestly and aptly by the author. This little book has so plainly been a labour of love that the reader cannot but love it also, and with it the benign and learned sage who has written it for us.

[3] *Science and the modern world*, Cambridge, 1926.

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NUTRITION IN NEWFOUNDLAND

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The nutrition of people in Newfoundland has attracted particular attention since Aykroyd, in 1930, reported on the incidence of beriberi and other deficiency diseases. Between 1941 and the end of 1944 three teams (McDevitt *et al*, 1944, Metcoff *et al*, 1945, Adamson *et al*, 1945), equipped with the latest methods of investigation, visited the island. The population of one third of a million must be one of the most fully studied in the world. All three teams found evidence of widespread malnutrition, although they saw no cases of frank beriberi.

The last of these teams submitted a report to the Commissioner for Public Health and Welfare in the Newfoundland Government. In this report they recommended methods of improving the diet, safeguarding the nutrition of children, and teaching the people to make better use of the food available. It was considered that, as a preliminary step, ways and means of approaching the problem in the field should be discussed with a skilled and experienced nutritional scientist. The Medical Research Council agreed that Dr. Cuthbertson should visit Newfoundland for six weeks in the summer of 1945. In this time he visited the chief town of St. John's and both the interior and several of the outports on the Coast, held discussions with representatives of the Health Service, the medical profession and the Nutrition Council of the Newfoundland Government.

Although Cuthbertson went primarily to advise, he was able to examine 260 persons, mainly children, clinically. He found the signs of malnutrition, reported by previous investigators, but, apart from dental caries, the signs were less frequent. For example, in the most extensive survey of 1944 (Adamson *et al*, 1945), mild follicular changes and follicular keratosis in 42% of subjects examined was reported, while Cuthbertson found those changes in only 15%.

Cuthbertson writes in his report[1]: "There is no doubt that observers differ quite markedly in their appreciation of what is and what is not a departure from normality." The significance of most of the clinical findings is very doubtful. Cuthbertson quotes Stannus (1945) who appears to consider that the "folliculosis", which the teams of the Ministry of Health have found in 15% to 35% of children, is the same as the follicular keratosis of, for example, Frazier & Hu (1931). But is this condition, which is so common in Britain, really like that illustrated by Frazier & Hu or the same as that found in Newfoundland? And, in the latter case, can the incidence in Newfoundland be regarded as evidence of any special degree of malnutrition? Like his predecessors, Cuthbertson considered that the physique of the men was poor. Children were up to standard in height, but their weights were low. The heights and weights of a group of pupil-teachers compared favourably with those of men and women in Britain, belonging to comparable groups.

In the second survey (Metcoff *et al.*, 1945) the percentages of women and children with some degree of anaemia was considerably higher than those found in Britain in the 1943 survey (Haemoglobin Survey Committee, 1945). Even with such more-objective signs, it may be difficult to form any conclusion, owing to differences in the methods used in calculation or presentation of the results. Thus, in the report of the third survey (Adamson *et al.*, 1945), the haemoglobin levels of a mixed group of children and adults are compared with those of children, age and sex unspecified, in a school in New York; although a haemoglobin level that would be low for a man may be normal for a woman, and one that would be normal for a child of 7 years would be low for a boy of 15. The specific gravity of serum was estimated by the gradient method of Linderström-Lang; the concentration of protein was calculated by the formula of Moore & Van Slyke (1930), although this formula does not express the relation between concentration of protein and specific gravity as estimated by this method. There may be insuperable difficulties in standardizing the clinical methods; but agreement could be reached on laboratory methods and modes of expressing results. This might be one of the first tasks of WHO.

Cuthbertson recommends that the diet might be improved in the following ways:

A. Milk. Among the major needs is an increased supply of milk. All possible land should be cultivated. An improved type of grass, which would afford grazing early in the spring and late in the autumn might be sown. The use of silage should be taught. Possibly food-yeast, which might be made from the sulphate waste-liquors of the paper-pulp industry, might be used as a protein-concentrate. Enough milk could be made available, as a result of the reduction of demands by the navy and of the amounts used for ice-cream, to supply every schoolchild in St. John's with ⅔ pint [0.38 l.] of milk per day. Until the amount of milk produced locally is increased, skim milk should be imported.

B. Vegetables. Interest in gardens should be stimulated. Curly kale, which will withstand the winter, should be grown. Recommendations are made for storing during the winter.

C. Animal Protein. The people of Newfoundland eat that very dull fish, cod, and use other more palatable and nutritious species for manure. Their supply of *animal protein* could be raised by eating these other fish. Greater use should be made of cod-liver oil and fish-waste. It might be possible to restock the island with moose and caribou.

D. Flour. Methods of improving the quality of the flour are considered, and preference is given to the use of a flour of 78–80% extraction-rate, fortified with 0.5% bone-meal. Iron and synthetic riboflavin should be added, and food-yeast used. The inhabitants might object to 78–80% flour, as they despise any but perfectly white flour.

E. Health education. Educational campaigns should stress the value of milk and the need to improve cooking, particularly of vegetables. It is suggested that vegetables should be eaten raw, but while teeth are so bad this is out of the question.

[1] [For particulars see *Book Reviews.*]

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Annotations & News

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WATER-SUPPLY

The importance of an adequate supply of water to any individual or community makes it surprising that the general literature on the subject is so scanty. In *The story of water supply*,[1] Mr. Robins has, however, produced a book full of erudition, showing evidence of wide travel and reading, with many illustrations, yet written for "the uninformed but interested laymen", which will for long be a standard work.

Water is mankind's most important and universal food, and it is natural that from the earliest times the development of human settlements should have been conditioned by the presence of an ample water-supply. Further, the recognition of the need that this supply had to be wholesome, within the limits of contemporary knowledge, led to the assumption that some divinity presided over the source. This ensured some degree of protection from casual pollution, and led eventually to the attribution of healing or magical qualities to many wells and springs.

Many of Mr. Robins' researches lead to interesting trains of thought. For example, it is sad to reflect that the inhabitants of Imperial Rome were supplied with wholesome water to the extent of forty gallons[2] per head per day, whereas this standard has once more become recognized as necessary only in recent times, and that the pump, widely used in the Roman Empire (there is an example at Silchester) fell out of use with the fall of Rome and was not re-introduced into Europe until the sixteenth century, and then mainly for the purpose of land-drainage. Again, although the slow sandfilter was not introduced until 1820 yet, in the seventeenth century, the citizens of Paris purified their drinking water, obtained from the Seine, by passing it through cisterns filled with sand.

Coming to more modern times, one is delighted to read that upon the inauguration in 1875 of a public water-supply at Trowbridge, the event was celebrated by sending a jet of water over the church-tower, but at the same time, one wonders what became of "Jinny Pumphandle" who presided for years over the older town pump.

To those of a modern generation who are accustomed to turn on a tap and to receive at once a plentiful gush of water, it must appear strange that most, if not all conduits, the main urban source of supply, during the XVI, XVII and XVIII centuries, were locked at night, while the Plymouth Dock Water Company in 1800 offered to its consumers a supply of water for two hours every second day.

Mr. Robins comments on the present practice of condemning any small well, supplying few people, whose water is not up to the standard expected by a large undertaking. He really answers his own question in a quotation he gives from Martin Lister, who wrote in the seventeenth century: "the water of the Seine is very pernicious to strangers . . . but the natives of Paris are not injured by it". Consumers in a more static age became inured to the casual pollution of their own water-supply: when visitors were few, no-one suffered ill effects from its consumption. Further, the presence of pollution in a water-supply does not necessarily mean that the bacteria are pathogenic, but that if any one type of bacteria can gain access so too can any lethal one that happens to be in the neighbourhood.

The gradual deterioration of the water-supply of London during the eighteenth and early nineteenth centuries is discussed at some length, and might not the statement made in 1726 by the swiss traveller, de Saussure, that in London "absolutely no water is drunk. The lower classes, even the paupers, do not know what it is to quench their thirst with water" be answered by the reply of the witness quoted by the Report of the Royal Commission on the Water Supply of the Metropolis in 1834—"We cannot drink the water, sir, it makes us ill".

* * * * *

From this historical survey of water-supply, it is interesting to pass to a study of the Report,[3] published by the Department of Scientific and Industrial Research, of its Water Pollution Research Board.

In this report, the first to be published since 1939, the Chairman of the Board refers to the many problems, particularly those concerned with the disposal of sewage and trade-effluents, that have been referred to the Water Pollution Research Laboratory for advice. These problems arose during the war-years because camps, in great numbers, had to be set up all over Britain, and new factories, some with new industrial wastes, had to be erected on what would normally have been thought unsuitable sites. It is a matter of gratification that the Department was consulted so frequently on these problems and of satisfaction that helpful solutions were so frequently found. With future industrial developments and the establishment of new towns the knowledge and experience gained by the Department will become increasingly useful.

To show the diversity of the work undertaken it is necessary to mention only the elaborate investigation that was carried out into the nuisance caused by excessive fly-breeding on the percolating filters of sewage-works, when the wholesale destruction of the larvae would have ensured the destruction also of the scouring organisms, springtails and worms, which are needed to remove from the filter the biological film that would otherwise choke it. Promising results from the use of DDT and Gammexane have, however, already been obtained.

Important work was done which showed that creosote in an earth-closet acted almost solely as a deodorant, and that the use of caustic soda in a chemical closet had practically no effect in diminishing the amounts of organic matter in the final effluent, and certainly had no sterilizing effect on solid faecal matter: the final disposal of the contents requiring as much care as if they were untreated excreta. Of equal importance, though not necessarily of such universal interest, is the discovery that by means of aeration it is possible to keep the highly-polluting effluent from a flax-retting[4] factory at a pH value of about 7, and that it is then possible

[1] [For particulars see *Book Reviews*.]
[2] [1 gallon = 4.54 l.—ED.]
[3] [For particulars see *Book Reviews*.]
[4] [Retting is a process for separating the fibres of flax from the woody part by soaking, macerating and other treatment.—ED.]

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While food is so scarce throughout the world it may be correct to force marginal cultivation. Although it will be necessary to subsidize milk, and possibly other foodstuffs, if they are to come within the purchasing power of the local consumers, would it not be right for the islanders, when food becomes more plentiful, to give up an unequal battle with a harsh climate and barren soil and devote their labour to the production of those commodities which the island is specially fitted to produce? Some persons have advocated the abandonment of the island but, as Cuthbertson writes, Newfoundland has a vital role to play in the world's need for animal protein. If they supply the world, the world should supply them with food that they cannot well produce at home. As the Hot Springs Conference declared, "the first cause of malnutrition is poverty". The islanders cannot afford to import what they need from abroad. At present both agriculture and fishing, like agriculture in peasant countries, are pursued in units that are too small. As Cuthbertson writes, if Newfoundland is to play its part in supplying the world, the entire fish-industry must be reorganized from top to bottom.

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for this fluid to be used many times for rets. Thus the quantity of final effluent is reduced to an amount that can easily be disposed of by spraying it on the land.

An important investigation into the effects of chlorinating the effluent from the Coventry sewage-works before its discharge into the River Avon had to be abandoned when it was discovered that the presence of a small amount of chlorine, considerably less than the chlorine demand, in the effluent, made this highly toxic. This is attributed to the combination of chlorine with thiocyanate, a regular constituent of an effluent composed, as so many are, partly of sewage and partly of effluent from gas works.

On questions dealing with the potability of drinking-water the Laboratory has been active. An investigation into the possibility of establishing a standard method of treatment for small supplies of lead-solvent water, usually from moorland sources, had to be abandoned owing to the war, but not before useful results had been obtained showing the value of finely-graded limestone-chippings from $\frac{1}{8}$ to $\frac{1}{16}$ of an inch[1] in size. But a simple method of removing the peaty film, deposited by the water on the chips, needs to be devised.

Owing to wartime shortages it was impossible to provide the elaborate aeration-plant necessary to enable certain iron-bearing waters to retain their iron in solution—if this iron comes out of solution the water becomes horrid in appearance and loathsome to taste and smell. It was found that the addition of sodium hexametaphosphate, in doses of about 2 parts per million, enables the bulk, if not all, of the iron to be retained in solution, and a considerable improvement in the potability of the water results.

One of the most useful and spectacular works carried out by the Department was the invention of a practical method of making seawater potable. This was of great value during the war, when sea-travel was hazardous, and many airmen were forced to abandon their craft in the sea and take to a rubber dinghy. For life-boats a still was designed, with a paraffin burner, from which it was estimated that a volume of drinking water ten times as great as the bulk of the paraffin, or 3.6 times as great as the bulk of the paraffin and still combined, could be made in a fortnight; the total amount of water per still being 60 gallons. For use in rubber dinghies, a chemical method of treatment was preferred, a method based on a silver compound of a base-exchange zeolite. When the zeolite was mixed with seawater, sodium was taken up by the zeolite, while the chlorine combined with the silver and was precipitated as silver chloride. The mixture was compressed into briquettes, to which a small amount of fuller's earth was added to help to break up the briquette when wet. As a result, an amount of drinking water 5.7 times the volume of the briquette was made available.

These are only a few examples, taken at random, from the Report. Much of the work has already been published in detail in scientific journals, and all is available to interested inquirers. The excellent results obtained show the value of a body with expert knowledge and reasonable facilities working, with considerable independence, under a grant from the Privy Council. Anyone may seek their advice, and this is freely and willingly given. In such a way scientific knowledge is used for the best purpose and for the direct benefit of the world. The discovery of such a multitude of practical and useful facts, and their application without let or hindrance whenever they are needed, shows science in its true perspective as a devoted and willing handmaid working towards the greater glory of mankind.

Amulree

[1] [1 inch = 2.54 cm.—ED.]

1132

ARE SYPHILIS, YAWS, BEJEL, AND PINTA MANIFESTATIONS OF AN ETIOLOGICALLY-IDENTICAL DISEASE ?

Treponematosis,[1] by Ellis H. Hudson, is a work of the highest interest to syphilologists in any country and to all men practising in warm climates. It is most stimulating and indeed gives one furiously to think. If the author's views are accepted, and they seem very convincing, he, a man of wide renown in tropical medicine, has done good service in simplifying a complicated subject, in correlating and reducing to one fundamental cause four syndromes or symptom-complexes, namely those of yaws, syphilis, bejel and pinta, concerning the first two of which there have for years been conflicting opinions: the unicists, the protagonist of whom was Admiral Butler, USN, maintaining that they are one and indivisible, and the dualists holding that they are separate and distinct. Etiologically—and causation is the safest ground for differentiating diseases—no distinction, morphological, serological or other, can be made between the treponemes found in all four. At the same time it must be remembered that the organism has not yet been cultivated artificially, and until it has we are justified in regarding them as one, and the symptoms produced as different manifestations of its activity, of treponematosis in short. It is wrong, and purely arbitrary to argue that because yaws and pinta are characterized by different symptoms, therefore the Treponema found in each, though apparently the same, must *ipso facto* be different. Cross-immunity experiments may help to solve the problem; it has been shown that syphilis seems to confer immunity to yaws, but the reverse of this has not, so far as the reviewer is aware, been tested,[2] nor whether pinta and bejel protect against syphilis.

Briefly, the author's thesis is this: In the moist tropics, treponematosis appears as yaws, a disease of the skin-surfaces, mainly of childhood, and non-venereal; in cooler and drier climates, as deserts and hill-districts, it affects normally the moist parts, axilla, fauces, perineum, vulva, forming mucous patches and again, mainly at least, non-venereal as bejel in Syria. In temperate climates, clothing covers most of the body and treponematosis is no longer primarily a skin affection but a mucosal one, and so passes from the juvenile non-venereal to the adult venereal form. Also, we see transitional treponematosis or "syphiloids" and "custom syphilis", in Russia for example, from promiscuous Easter kissing, kissing of ikons, and use of cups in common. All transitions between yaws on the one side and paresis (so-called parasyphilis) on the other can be traced. If yaws comes to a temperate climate it does not remain as yaws but as syphilis. The author gives an excellent and clear comparison between yaws, bejel and syphilis (pp. 64-67). The oft-repeated pathological differences between the forms of treponematosis are shown to be quantitative, not qualitative, "differences in degree, not in essence." Cutaneous dyschromia occurs not only in pinta, but in all the others. "It is one of the late hall-marks of the juvenile, untreated form of the infection."

Strains of an organism. Treponema or other, all can accept, but, asks the author, at what point does a strain become so differentiated from its fellows that it becomes a species? The difficulty is increased if there is the possibility of the new form slipping back to the original. Even granting that the different syndromes are caused by different strains of the same species, they are still merely variations of one disease. The author uses freely the term "clinical entity"—a term abhorred by Sir Clifford Allbutt—in spite of his defining an entity as "an independently existing thing." In the reviewer's opinion, syndrome, symptom-complex, or even symptomatology is preferable to an "independently existing thing" which cannot exist independently of a body—the patient—in which to exhibit and exert its effects.

We have abundant evidence that diseases may change their type. Scarlet fever, highly fatal less than a century ago, is now so mild that one hears a mother say "It was not scarlet fever at all, it was just scarlatina." Smallpox, even in epidemic form, in the tropics may be mild, as alastrim, or very severe and fatal. As the non-venereal type of treponematosis becomes the venereal, so the *sibbens* of Scotland, the *button-scurvy* of Ireland, the *radesyge* of Scandinavia and the *skerljevo* of Dalmatia show a reversal from the venereal to the non-venereal form, from syphilis-like to yaws-like.

To sum up: Yaws, bejel, pinta and syphilis are syndromes, not separate diseases, and even as syndromes they are not altogether distinct, but overlap. Fundamentally, that is etiologically, they are one; epidemiologically, as the result of environment and interaction between invader and invaded, they differ, and we can trace the progression from the earliest juvenile, non-venereal yaws, through the transitional, usually non-venereal, bejel and pinta to the adult venereal syphilis of civilization.

There are several other points one would like to discuss, but lack of space forbids. The work may be strongly recommended; the author has earned the thanks of a wide circle of readers and is to be heartily congratulated on the clarity of his exposition.

H. Harold Scott

[1] [For particulars see *Book Reviews*.]

[2] [In *British Medical Bulletin*, 1945, 3, 197, a report (*BMB* 772) was published of an original experiment by G. M. Findlay and R. R. Willcox. These workers succeeded in producing a penile lesion by inoculation with *Trep. pallidum* in a patient who had recently suffered from active tertiary yaws, and who possessed positive serological reactions due to the yaws infection.—ED.]

1133

GRUNEBERG AND DARLINGTON ON GENETICS

Those of us who have one foot in genetics and the other in medicine have long been saddened by the knowledge that between these two fields of scientific enquiry there has in the past been far too little intercommunication. Whilst geneticists have been studying the action of the gene and the mode of inheritance of "characters" in their experimental animals of choice, those engaged in medical research have been seeking an understanding of the cause and of the mechanisms of development of human "disease", and quite commonly the character of the geneticist has been either very similar to or even identical with the disease of the medical investigator. So it is that, sometimes quite unknown to medicine, there has been accumulated in genetical literature a considerable volume of established fact which has a very direct bearing upon medical research and which, becoming known to the medical pathologist and clinician, would undoubtedly bring to him great reinforcement and a much greater understanding of his own problems.

Though, during recent years, the liaison between these two groups has been steadily improving, even yet medicine has been too little affected by genetical discovery. One reason for this has been that genetical enquiry in the main has until recently been dealing with the nature of the gene itself, rather than with the nature of its action upon the processes of development and degeneration.

Amongst those who have been most active in the field of physiological genetics is Hans Grüneberg, whose work has been so grievously interrupted by the circumstances of war. But even his wartime medical duties could not entirely satisfy his interests or consume his energies, for in 1943 there appeared a product of his pen, a magnificent volume on the genetics of the mouse, and now there appears his long-awaited book[1]—*Animal genetics and medicine*—on the attractions which his own variety of genetics should have for medicine. With the appearance of this book there can no longer be any excuse for a lack of appreciation on the part of embryologists, pathologists and clinicians of the value of the contributions that genetics has to offer them. It sets out to evaluate inherited diseases as dynamic processes, and concerns itself almost entirely with the physiological channels by which the genes produce their end-results. The author shows in very brilliant fashion that the material of choice for the proper study of mankind is not always man, in whom genetic homogeneity can seldom be secured, who mates as he wishes, whose environment cannot be equalized, in whom inherited disease of the more obvious and simply-transmitted kind is rare, and in whom also the earlier stages of any pathological process cannot be intimately examined.

Dr. Grüneberg's argument, which he easily sustains, is that in a great variety of instances it would greatly advantage the pathologist and clinician interested in the etiology and manner of development in such a condition, for example, as harelip and cleft palate, to turn from man to the mouse, in whom this very condition is known to be a genetic character and simply inherited. The number of its exhibitors in the mouse can therefore be as numerous as investigation demands, since by appropriate matings any given number can be obtained; and since the mouse may be slain and examined at any point in its life-history, each and every stage in the development of this abnormality can be examined and recorded. What is true for harelip holds equally for a very large number of the more-puzzling and distressful abnormalities encountered in human medicine and which as genetical characters have been thoroughly studied—certain of the anaemias, endocrine disorders, locomotor disturbances and a great diversity of congenital and other defects and derangements which cover the whole range of the organs and organ-systems of man.

This book should have a very considerable effect upon developments in medical research, since in the storehouse of genetical literature there is a great mass of information which has a very direct and immediate bearing upon a very wide variety of medical problems. Though its production leaves something to be desired and its cost is high, it is a book which must not be disregarded by such as are seeking an understanding of the development of human anatomical and physiological abnormality.

[1] [For particulars see *Book Reviews.*]

We in Britain have been singularly fortunate in that genetics has always attracted some of the best minds in biological science. At the turn of the century there was Bateson, a very great figure, and from him there sprang a line which has always succeeded in maintaining the great reputation of british geneticists. J. B. S. Haldane, R. A. Fisher and C. D. Darlington are names which, like that of Bateson himself, have become woven into the very fabric of genetical science. They are but few compared with the geneticists of like ability who have enjoyed so much greater opportunities in the United States of America, but the importance of the contributions that they have made to the development of genetical theory is not surpassed.

Darlington's *The evolution of genetic systems*, first published in 1939 and now reprinted[2], shows the great quality of Darlington's mind. Cultured, well stored with scientific fact, using fact as an invitation to thought and adventurous speculation, bold, somewhat aloof, imaginative beyond the ordinary, iconoclastic, perhaps finding a certain pleasure as it soars in flight in disregarding the criticisms of such as insist on keeping their feet well sunk in the mud of current orthodoxy, it has predicted time and time again that which later the critic himself has reluctantly found to be so.

An irritating person this, who because of his stature can see what to the rest of us remains hidden. To be so often right is to attract both praise and abuse, and Darlington has received a great deal of both—not that either has bothered him or caused him to pause as he has proceeded to construct his hypotheses.

This book of his is one of the outstanding contributions to biological synthesis that has appeared during the last hundred years. It is a small book, for Darlington does not waste words, but it is crammed with arguments and ideas; ideas that are of the greatest importance in that they corrode the barriers between the several compartments of biological science—even between the physical and biological sciences.

It is no book to read at all easily; it is one to be studied closely, and it merits the most careful study. It is recommended that it should be approached with the intention of disagreeing with almost everything it says. But the reader must be warned that, if fairness is maintained, it will be exceedingly difficult to end it and still find that one remains unconvinced as to the essential reasonableness of it all.

Admirable is the man who can cultivate such ideas and present them in such fashion.

F. A. E. Crew

1134

PROGRESS IN THE WAR AGAINST THE LOUSE

The literature concerning the arthropods parasitizing man is widely scattered in numerous scientific journals, not necessarily medical, and written in many languages, while the more important the parasite and the more widespread its distribution, the more extensive become the records of those who have studied its bionomics and control. Under certain circumstances one or more of these parasites may assume, quite suddenly, special importance, in which case it becomes not merely desirable, but essential that some scientist, whose training and knowledge have specially fitted him for the work, should undertake the onerous task of sifting the existing knowledge of the subject and presenting the results to those responsible for applying it to the best advantage. In past wars the louse, in its capacity as a vector of epidemic disease, has always assumed a position of great and sometimes of predominant importance, and hence the opportune appearance of Professor Buxton's book on *The louse* at the outbreak of the recent war. A reviewer of the first edition wrote in 1939,

> "The war of 1914-18 called forth in all countries an immense output of research on the louse—its biology and the best means of combating it under war conditions. The 20 years which followed, although they have added much to our knowledge of the louse-borne diseases, have added almost nothing to the efficacy of existing methods of louse control. With the renewed outbreak of war the louse will again become a military problem—how important a problem will depend upon which of the louse-borne diseases make their appearance among the troops."

To that might be added: and in how short a space of time we can augment our existing scanty knowledge of louse-control! That this essential knowledge was forthcoming in time to prevent any serious outbreak of louse-borne disease amongst british or

[2] [For particulars see *Book Reviews.*]

american troops on any battle-front is now a matter of medical history and justifies the author's comment, in a recently-published 2nd edition[1] of his book :

> "The efficiency of DDT in controlling body and head lice, even under extremely bad general conditions, is so great that perhaps we have now seen the last great typhus epidemic."

This is a fine achievement and one to which the author of the book has contributed no small share. As a result of this advance in knowledge during the war years, Buxton's book has grown from 145 to 164 pages, each of which contains considerably more type than did the first edition, and the chapter entitled "The control of lice" has had to be completely re-written, ". . . for what was said in the first edition has now nothing more than historic interest"; while the section devoted to the collective biology of the louse has also been considerably expanded. The 1947 edition is printed on considerably thinner paper than that of 1939, so that the increase in print has caused no corresponding increase in bulk, indeed, the new edition is a more slender volume.

The amount of work involved in writing this book and in bringing it up to date must have been great, but the result is worth while and may encourage others to do for, let us say, the bed-bug, what Buxton has done for the louse and Heilesen for the itch-mite.

R. M. Gordon

[1] [For particulars see *Book Reviews*.]

1135

A NEW KIND OF MEDICAL TEXTBOOK

Dr. A. E. Clark-Kennedy's *Medicine*[1] (Vol. I, *The patient and his disease*) is not just "another text-book of medicine". Its author is alive to the defects of existing manuals and seeks to provide the remedy. The rapid growth of medicine and of its complicated techniques of diagnosis and treatment have determined the shape of present-day clinical instruction. The student is taught by experts in a limited field; patients are too often segregated in hospital into groups according to the principal site of their disease (e.g. heart departments), or to functional disturbances (e.g. allergic and diabetic clinics), or to the form of treatment proposed (e.g. medical and surgical wards). Modern text-books reflect this compartmentalism. They assemble contributions from many sources, excellent in themselves but lacking correlation and integration. Notions of "disease" which are equally applicable to, say, peritonitis and meningitis are unheeded or disregarded; instead the writers provide detailed descriptions of "diseases"; unmindful that a convenient label is a flimsy foundation for rational understanding. Thus, for the student, medicine comes to resemble a patchwork quilt with many gaps when what he needs is a tapestry of continuous, clear and purposeful design. For he must study man as a whole, as a sentient being who is more than the sum of his parts.

The aim of this book is to correct the faults of a fragmented medicine, to emphasize the general principles which underlie the phenomena of disease, and to describe the elements of the methods of medicine as a foundation on which to build securely as knowledge grows and experience deepens.

The first volume treats of *The patient and his disease*. It opens with a chapter on Body and Mind, in which is attempted a synthesis of the basic preclinical sciences which Dr. Clark-Kennedy rightly holds to be an indispensable introduction to clinical medicine. This is perhaps the least-successful chapter in the book. It is not possible to compress so much into the space which the author permits himself for the statement of this part of his thesis. The second chapter deals with Symptoms. In it is emphasized the imperceptible transition between health and disease, and how artificial is the separation of symptoms and signs. Here also are described the methods by which a patient's complaints, both mental and physical, are elicited, and how they are to be interpreted in terms of disordered function, structure and mind. Fatigue—mental and physical—pain, indigestion, shortness of breath, fever, flatulence, repeated vomiting, giddiness, faints and fits, chronic constipation and diarrhoea, gain and loss of weight, bleeding and other discharges from the body's orifices, are among the examples quoted to show that symptoms and signs arise from derangement of normal physiological mechanisms; their causes are illustrated from all branches of medicine. In the third chapter the information which a detailed physical examination reveals is subjected to similar analysis.

[1] [For particulars see *Book Reviews*.]

The fourth chapter is an admirable essay on the influence on man's life (and death) of Heredity and Environment. It will surprise the orthodox to find a description of intrauterine development in a textbook of medicine, but if human life and its ills are to be reviewed and a continuous story unfolded, the start is in the fertilization of the ovum and the end is in the grave. The interplay of nature and nurture is reviewed in assessing the effects of nutrition, accidents, chemical substances and other forms of life on the genesis of disease; and their influence on such diverse features as a man's personality, philosophy, religion, deformities, ageing, degenerations, neoplasms and the rest, is reviewed.

There follows in chapter V a description of mental and bodily reactions, both physiological and pathological, to changing demands and altered environment. Physiological adjustments, hypertrophy and atrophy, inflammation and allergy, anxiety and fear, escape-mechanisms and self-deception are but a few of the reactions examined. The final chapter attempts to define the Nature of Disease. It embodies the author's thesis: "Pathology is the study of the interaction between the genetic endowment of man, his way of life, and the environment into which he has been born. There is a pathology of the body and a pathology of the mind. Each has inevitable repercussions on the other . . . A pathological process of the body is the action of some factor which exerts an adverse influence directly on or in the body and the natural reaction by the body. Some pathological processes arise from defects in the genetic plan whence the individual is derived. Others arise as the result of life in the environment." The seven pathological processes which he recognizes are congenital defects, nutritional failure, trauma, chemical poisoning, infection, neoplasm and degeneration. All these are of the same physico-chemical nature as the body. Disease represents disturbances at the level of the body's physico-chemical reactions, though it may also start at the metaphysical level of the mind.

It would be idle to claim that Dr. Clark-Kennedy's thesis is here adequately summarized. It does not easily lend itself to compression. Indeed, if there be any valid criticism of this work it is that its author has crammed too much into too small a compass. Some of his statements are so condensed as to be misleading. His explanation of visceral pain (p. 65) is inadequate and outmoded. Does colonic pain "travel round the abdomen"? And does cardiac pain "compel the patient to stand still under almost any circumstances" (p. 66)? Would many agree that: "Gall-stone dyspepsia is probably a myth" (p. 71)? Will the novice profit from the "potted" version of philosophy and religion on pp. 219–223? But it is ungracious to raise minor and immaterial points of criticism for here is a most thoughtful and scholarly work, written in an engaging, vivid style, which presents the philosophy of medicine with exhilarating freshness. It will not yet supersede the standard textbooks of medicine for there are still examinations to pass. But the attitude of mind which this book seeks to inculcate will endure when many of the "facts" of medicine are forgotten. To the senior student and to the practitioner it can be recommended without reserve. A second volume on *Diagnosis, Prevention* and *Treatment* is promised shortly.

Henry Cohen

1136

DESPOTISM IN THE FAMILY

In a small book[1] on *The psychology of the unwanted child*, Dr. Agatha Bowley deals with great themes. Her aim is to reach the minds and to influence the practice of all those who are placed in charge of outcast children, so that these new guardians may ". . . recognise the supreme interest and importance of their task . . ." She is well fitted by her writings, study and practical experience, to offer advice of this kind. Although aware of the complexity of the subject, she tries in this book to give her readers practical suggestions and simple explanations.

In the first two chapters she deals first with the essentials of a good home where there is a right personal relationship between the parents and the children; and then with the disastrous effects of parental neglect on the personality of the child. These two chapters are a brief, fragmentary, and rather unsatisfactory analysis of the happy and the unhappy family. On this preliminary background there is drawn, in greater detail and with interesting documentation from her own studies, the picture of the unwanted child, often already showing deep marks of injury in character and

[1] [For particulars see *Book Reviews*.]

behaviour; and of the problem of re-adjustment of the child in the substitute-home, whether adopted, boarded-out, or in institutions.

The psychology of the child, whether with steady or with shaken personality, is a vast and profound subject; and the science of this dark continent of child-psychology is itself in its infancy, not yet sure or clear in its language, nor equipped with authoritative and accepted doctrines. But the exploration of the child-mind is being steadily pursued by scientific methods, and much new knowledge has been won. Under the surface of child-behaviour, the motives and meanings of this behaviour have been disclosed in child-play and dreams, and by other methods of investigation; and this understanding of hidden motives has given many clues for treatment and re-adjustment.

But the deeper mysteries of the influences that pass to and fro between mother, father, and children are the primary causes that shape the developing personality of the child; and these mysterious currents of influence require much more study and clearer enunciation. Those deep and obscure forces that determine the happy or unhappy destiny of children are only briefly mentioned and glanced at in the book. This is not put forward as a fault or criticism in a book which has more immediate and practical aims; but it is a warning against too hasty and confident application of unproved theories and speculations to clinical practice.

In fact, this little book raises, although not dealing fully with them, the ultimate issues of human welfare and happiness—issues that are being continuously decided all over the world in all the families of mankind. Neither can these great issues be properly discussed in this review; but a brief and scrappy final comment may be made. The present wide-spread dissolution and destruction of human families which shows itself in many ways, and especially in the increasing numbers of unwanted, uprooted, and "displaced children", has many causes. What we are witnessing today in so many of our families of every class, is, in social and political terms, a condition of civil anarchy in the family. This anarchy is due in part to the breakdown of the principle of monarchy in the family "state". Monarchy in the family is the strict unquestioned rule of parents (mother and father) over the child; and the little child thrives best in the air of despotism. Without this loving despotism of the parents, the child turns towards spiritual anarchism, becoming a law unto himself, and missing the two primary "goods" of human life—control of self and consideration of others. But today despotism is a hated word, and discipline is out of favour. The monarchical principle in family life does not seem to be favoured by Dr. Agatha Bowley, and in her explanations of causes and remedies little mention is made of strict rule and discipline in the family.

1137

COLOUR-VISION

Two recent books on colour-vision report their authors' original work and theories, presented in a general review of the subject as a whole. But although both are concerned with the same subject-matter, their approach is quite different.

Dr. W. D. Wright's *Researches on normal and defective colour vision*[1] is mainly concerned with a detailed report of experiments carried out by himself and his colleagues since 1926. The first forty pages give a brief review of the physiology of vision. The next section gives details of colorimetric equipment used in the experiments and a description of the methods of operation and calibration. The experiments reported are concerned with determinations of the luminosity-curves, colour-mixture, visual discrimination and adaptation-phenomena, and research on defective colour-vision.

Many of the experiments confirm earlier work but, by the use of improved apparatus, provide results with a more precise and intelligible meaning. In his account of this work he provides details of experimental technique and analysis of results. While the book is primarily of interest to the research-worker, the many different lines of enquiry are reported in such a fashion that their relation to earlier work, and their importance in an understanding of the physiology of colour-vision, are made clear.

Dr. Wright is well aware of the pitfalls that await those who traverse the ill-defined territory between physics, physiology and psychology. "If the acrimonious discussion and misunderstanding which has existed in the past is to be avoided in the future, it is of the greatest importance that the limited nature of the deductions which can be legitimately made about the colour perception mechanism from colour matching data, should be recognised."

Perhaps he clings to this opinion too rigidly, since a little more speculative interpretation of his results would have done much to leaven an otherwise commendable detail and precision in their statement.

By way of contrast, Dr. E. N. Willmer's *Retinal structure and colour vision*[2] seems to strike an admirable balance between fact and theory. He puts forward a new interpretation of existing data on the physiology of colour-vision and shows a delightful ability to use a theory to its best advantage without becoming blind to its deficiencies. He is deliberately speculative for he believes that ". . . . the purpose of a hypothesis is to stimulate thought and research, not necessarily to be right in the first instance."

It has become almost a tradition in visual physiology to postulate four different types of light-sensitive receptor in the human retina —the rods, operative only at low intensities, together with three types of cone each peculiarly sensitive to bright light of either a red, blue or green colour. Dr. Willmer, as a histologist, re-examines the data in support of such an hypothesis and concludes that ". . . an undue weight must not be placed on the negative histological evidence, but at the same time the evidence *is* negative and that in spite of over a century of research directed towards the demonstration of different cone types."

He shows that the two well-known visibility-curves for the light-adapted and dark-adapted eyes are sufficient, with certain reasonable assumptions, to explain many of the accepted data on colour-mixing. These two visibility-curves are usually regarded as representative of the individual rod- and cone-sensitivities. This leads him to the main theme of his book, which is an admirably-balanced discussion of how far the existence of two functionally-different receptors, the rods and cones alone, will go towards explaining the known facts of colour-vision. The investigation certainly ". . . provides for the first time, an opportunity for describing many of the phenomena of colour-vision in a quantitative manner, which is at the same time related to the physiological basis of vision." After an almost spectacular success with his original hypothesis, he is ultimately forced to postulate a third type of receptor-cell, with maximal sensitivity to blue light, which although a rod, is unable to adapt itself to darkness.

Whether or not all of the assumptions made in this book stand the test of time and further experiment, seems less important than the fact that they are bound to give new vitality to a subject which at times seemed badly in need of some such medicine.

[1] [For particulars see *Book Reviews*.]

1138

WORK OF THE LISTER INSTITUTE

The annual report[1] was presented by Sir Henry Dale, chairman of the Governing Body, at the annual general meeting, 20 June 1947.

Bacteriological, Immunological and Pathological Studies.—An examination of the virulence, colony-appearance and capsule-formation of *H. pertussis* is being undertaken to see if this organism undergoes dissociation due to inherent or environmental factors, and to determine whether any of these factors influence the immunizing potency of vaccines. An investigation of gas-gangrene antitoxin extracted from the tissues of rabbits, guinea-pigs and rats immunized with *Cl. welchii* toxoid has shown that in all three species the lung has the highest antitoxin-content relative to the serum-titre. The chemical properties of the hydrolysates produced by hydrolyzing purified potassium hyaluronate with hyaluronidases have been shown to differ according to the source from which the enzyme has been obtained. Experiments to decide whether hydrolysis was brought about by a single enzyme or by a number of enzymes acting in series suggest that, in the case of streptococcal and staphylococcal hyaluronidase, more than one enzyme is involved. Work on the nuclear structure of bacteria has been carried out, and observations have been continued on pyrogens and other reacting substances in material used for transfusion. Batches of dextran prepared at Birmingham University have been tested for their antigenic and blood-pressure-restoring properties, and have been found closely to resemble swedish dextran.

[1] [For particulars see *Book Reviews*.]

Studies on muscle-ischaemia suggest that the maintenance of the cycle for the metabolism of carbohydrate is a crucial factor in maintaining the normal permeability of the muscle-fibre, and that the changes leading to clinical shock after the release of a tourniquet may arise from failure to re-establish this cycle. The results of work on trichomoniasis in cattle, including the re-infection of animals which had infections of varying severities, indicate that subclinical infections convey no immunity. Successful bulk-production of *Trichomonas foetus* has been achieved.

No method of eliminating the bacterial flora of vaccine-lymph has been found which does not also reduce the amount of the virus. During investigations on this subject it was found that certain bacteria enhanced the proliferation of vaccinia-virus in experimental animals, this adjuvant effect apparently being proportional to the hyaluronidase produced by the organism. Furthermore, spread of bacteria appears to be proportional to hyaluronidase-production when staphylococci and virus are injected together, but not with staphylococci alone. The adjuvant action of hyaluronidase-producing streptococci and the virus appears to be even more striking. In a study of the formation of penicillinase by organisms of the subtilis group it has been shown that maximum production of this enzyme is obtained only when penicillin is added continuously during the growth-phase of the bacteria, and depends on adaptation during growth followed by lysis. The possibility of producing an antiserum against staphylococcal penicillinase is being investigated in view of its possible therapeutic value.

Biochemical Studies.—Investigations on the specific blood-group substances have shown that the electrophoretically homogeneous A-substance previously isolated from commercial hog-mucin and possessing both O- and A-specificity is in fact a mixture of two mucoids. The chemical and physical techniques employed were unable to separate the specific A and O blood-group substances from mixtures in which these mucoids occur. The A-, B- and O-substances occurring in pseudo-mucinous ovarian-cyst fluids have been further investigated, and the relationship between the reactivity of erythrocytes of all human groups to agglutination with anti-O sera and the capacity of individuals to secrete the so-called O-substances are being studied.

A member of the staff working in the Fysikalisk-Kemiska Institutet, Upsala, studied the adsorption-properties of gramicidin and tyrocidine. The former appears to be homogeneous when examined in alcoholic solution by the "front analysis" technique of Tiselius. Tyrocidine proved not to be homogeneous. A further quantity of the O-somatic antigens of *Bact. shigae* has been isolated, and methods suitable for its step-wise degradation are being elaborated. Work has continued on the "non-agglutinating" antibody, and has included the formation in rabbits of this type of immune body after injection of small quantities of *Bact. shigae* and of its purified O-somatic antigen and specific-polysaccharide and conjugated-protein components. Methods for the isolation of the main antigenic component from *Trichomonas foetus* have been elaborated.

Biophysical and Physico-chemical Studies.—Continued study of the purification of human fibrinogen has been specially concerned with the proportion specifically clotted by thrombin, and with the content of active and unactivated proteolytic enzymes. The interaction between tetanus toxin and antitoxin has been the subject of further study and, with a view to obtaining antitoxic sera showing only one end-point by flocculation, horses have been immunized with purified toxin and with toxin-antitoxin floccules.

In connexion with freeze-drying, the vacuum sublimation of ice in a tray-drier has been studied; the rate of vaporization per unit area per unit time, although 2 to 4 times greater than that in the centrifugal and transfusion-bottle driers, is only 1/400th of the ideal theoretical maximum. The apparent anomaly is related to the fact that molecular collisions with the condenser-surface are not all effective in condensation, the condensation-coefficient being less than unity. An ultrasonic generator has been constructed in which X-cut quartz disks are excited to vibration at the resonant frequency 500 kc./sec.—1 mc./sec. by application of high radio-frequency voltages. An investigation of the influence of ultrasonic vibrations on the protein molecule is being undertaken. Electrophoretic analyses of sera and serum-fractions from foetuses and newborn lambs of ewes kept at different levels of nutrition have been carried out. Osmotic studies of haemoglobin have continued. The unit for the preparation of plasma-products administered by the Medical Research Council has been in operation during the year and has maintained a steady output of human fibrinogen, fibrin and thrombin. Since October 1946 there has been a regular output of dried plasma for transfusion. A procedure for separating the immune-globulins from human plasma has been developed.

Nutritional Studies.—Further experiments on the nutritive value of wheat-proteins indicate about a 25 % advantage for the proteins of the whole grain over white flour of 70 % extraction.

Nicotinamide and Related Compounds.—It has been shown that, in pure and mixed cultures, growth, acid-formation and the production of nicotinamide by *Bact. coli* were stimulated by "ambamide" (*p*-amino-methyl-benzene-sulphonamide) in smaller concentrations and inhibited by larger concentrations, while nicotinamide-consuming bacteria such as *Proteus* and *Streptococcus* were inhibited by it even in small concentrations. Investigation of the contribution of intestinal bacteria to the nicotinamide requirements of man showed a parallelism between the relative densities of the *Bact. coli* population of the gut and urinary elimination of nicotinamide methochloride, both of which were considerably decreased after succinyl sulphathiazole and increased after ambamide intake. Biochemical examination of a patient with "black tongue" following oral pencillin showed that oral administration of penicillin to this patient, whose nicotinamide-status had been low beforehand, caused acute nicotinamide-deficiency which ceased after the discontinuation of penicillin or after administration of nicotinamide, but recurred with resumption of oral penicillin administration.

The Medical Research Council external scientific staff have continued their bacteriological, nutritional and blood-group studies. These have included analysis of the stages of tryptophan injection, the production of immunizing antigen in anthrax-cultures, the exploitation of *M. lysodeikticus* as a source of enzymes liberated from the cell, and further investigation of the Rh blood-groups. The National Collection of Type Cultures, whose original curator Dr. R. St. John-Brooks retired in October 1946, supplied more than 7,000 cultures to workers at home and abroad.

The Blood Group Reference Laboratory of the Ministry of Health has been concerned with the supply of standard A, B, O and Rh blood-grouping sera, and has been prepared to supply the rarer type of sera required for blood-grouping work.

The report records the deaths of several members, including Sir Joseph Barcroft, Sir Almroth Wright and Dr. H. L. Schütze.

L. T. Morton

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AN ARGENTINE VIEW OF BRITISH MEDICINE AND SCIENCE

Ciencia británica (Editorial Bajel, Buenos Aires, 1946) by Prof. Mariano R. Castex, of the Academia Nacional de Medicina, contains the text of six lectures delivered to the Asociación Argentina de Cultura Inglesa during the years 1940, 1941, 1943, 1944 and 1945. The first two lectures review the contributions made to medical progress by british medicine and science, and the lecturer gives short biographical sketches of some of the outstanding personalities among british doctors and scientists since early times. The three following lectures tell briefly and lucidly the story of the foundation and development of the Royal Society, the Royal Institution and of the medical schools of Oxford and Cambridge Universities. The final lecture gives an account of the founding and work of the Cavendish Laboratory at Cambridge and of its most outstanding achievements.

The paper, type and format of this book, which contains 208 pages, add greatly to the pleasure of reading it.

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JOURNALS NEWLY RECEIVED

Notes on journals recently received for the first time, usually in exchange with the British Medical Bulletin

Revista dell'Istituto Sieroterapico Italiano (Napoli) was previously known as the *Revista de Bioterapia e Immunologia*. It is published in two separate parts, one of which deals with biological and experimental work, the other containing articles of practical medical interest. The present number (Vol. 22, no. I, January-March 1947) contains original articles on the history of penicillin

and its chemical and biological properties (E. B. Chain), streptomycin in the treatment of tuberculosis (C. Jandolo), the prolongation of the therapeutic effects of penicillin by a new method, i.e. by injection of the drug in a subcutaneous area (thighs) where a venous and lymphatic stasis has been provoked by the use of a tourniquet (E. Carlinfanti & F. Morra), penicillin in the treatment of blepharitis and dacryocystitis by F. Fontana, restoration of anti-diphtheric immunity by oral administration (M. Petrini), and non-demonstrable serological incompatibility in a case of apparently typical haemolytic disease of the newborn (E. Carlinfanti).

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Of four czechoslovak journals received, the first is the attractively-produced *Rozhledy V Tuberkulose* (Prague), a publication of the Masaryk League for the Prevention of Tuberculosis. The journal is edited by Professor Skládal. Several of the contributions have summaries in English, and in each number there are very adequate reviews of two or three foreign books and articles bearing upon tuberculosis. Vol. 6, no. 4 contains an article on rehabilitation-methods at Papworth by R. R. Trail.

Pediatrické Listy (Prague) is the organ of the Czechoslovak Paediatric Society, and is published by the "Society of the Younger Generation of Doctors". It is edited by a board of nine, the chief editor being Dr. V. Baudiš, and appears six times a year, the annual subscription being 200 crowns [£1]. The main articles appear in Czech, with résumés in Russian, English and French; the subjects in this number include acrodynia; infectious diseases and neuropathic constitution; dysostosis craniofacialis (Crouzon); penicillin in the treatment of diphtheria; vitamin C in the treatment of pertussis; infant-mortality in Czechoslavakia. There are also abstracts of paediatric publications from USA, Switzerland, Sweden and Britain.

Sociální Revue is the organ of the Ministry of Labour and Social Welfare, and is edited by Dr. V. Berger. This is a monthly publication, price 8 crowns [10d.] for single numbers, annual subscription 90 crowns [9s.]. The main articles are printed in Czech, with abstracts in Russian and English; in this number they deal with trade-unions, social welfare, rehabilitation of victims of war and enemy persecution. Shorter notes are followed by a section on bibliography which lists publications from various countries on problems of social welfare, labour-conditions, food-control, etc.

The fourth of these czechoslovak journals, *Československá Gynaekologie* (Prague, vol. 12, no. 5) gives summaries in English of the three main articles on the use of pentothal in gynaecology and obstetrics, treatment of pemphigus neonatorum, and eclampsia during the war, the latter giving comparative figures for pre-war and war years. The journal concludes with reports of scientific meetings, therapeutic notes, reviews of literature, the contents in English of the *Journal of Obstetrics and Gynaecology of the British Empire*, vol. 53, no. 6, December 1946 and european news-items.

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Folia Gynaecologica (Genova, vol. 41, no. 3, 1946), a gynaecological journal from Italy, has been received. It contains 262 pages, and three articles are included, the first of which by Dr. Marion Ripetti discusses the advantages of reducing to the minimum the length of time patients remain in bed after gynaecological operations, and the circumstances in which it is advisable for them to do so. The second article deals with the histopathology of the placenta in toxaemias of pregnancy by Drs. Luciano Cirio & Marino Feraboli, and the third article is a study of hormone therapy in gynaecological disorders by Dr. Stelio Bonavita.

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Zdrowie Publiczne Miesiecznik (vol. 63, nos. 1-2-3, 1947) a journal from the State School of Hygiene, Warsaw, is published in Polish with an english list of contents. Articles cover preventive medicine and epidemiology with emphasis on tuberculosis and the work of the National Health Council in Poland. Interest is not, however, limited to Poland. This number goes further afield with papers on the anti-tuberculosis campaign in Germany, diphtheria epidemic in Europe, and population-problems in Finland. There are reviews in Polish of british public-health text-books.

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The first numbers of a new hungarian journal, *Orvostudományi Beszámoló: Diurna Medicinalia*, have reached us from Szeged. The chief editor, Professor Béla Purjesz, professor of medicine at the University of Szeged, states that its purpose is to inform hungarian doctors about recent researches and new books, and if possible to give accounts of papers read at congresses. If original articles are wanted by anyone in connexion with research, photostatic or typewritten copies will be supplied on request. The Minister of Education, Julius Ortutay, welcomes the effort in a foreword to the first number. The contents include review-articles, abstracts of articles in foreign journals, and book-reviews. No. 3-4 lists forty european, scandinavian, british and american journals from which articles are abstracted. The material in this new monthly periodical appears to be of a high standard, although production and paper are not very good and there are many typographical errors. The editorial office is at the Medical Clinic, University Hospital of Internal Diseases, Szeged, Hungary, and the annual subscription is 120 hungarian florins [*c.* £3]. It is published by the Free Trade Union of Hungarian Doctors, and all the editorial officers are professors and assistants of the University of Szeged.

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Another hungarian publication recently received is the official journal of the Hungarian Pharmaceutical Society: *A Magyar Gyógyszerésztudományi Társaság Értesitője*, which with volume 21 (1947) resumes publication after a lapse of two years. This contains original articles, in Hungarian, of pharmacological and pharmaceutical interest, and abstracts of articles in foreign journals, chiefly of pharmacological interest. It also publishes the Minutes of the Hungarian Pharmaceutical Society, and no. 3-4 includes reviews of hungarian, german and swiss books. This number contains amongst its original articles the text of a lecture given by Dr. Pál Turi on penicillin and other antibiotics; a summary in English is given of this article, which is chiefly based on the following monographs: Fleming, *Penicillin*, London, 1946; Herrel, *Penicillin and other antibiotics*, Philadelphia, 1945; Council of the Pharmaceutical Society of Great Britain, *Penicillin*, London, 1946. The journal is edited by Dr. Pál Lipták, professor of pharmacological chemistry, University of Budapest; the editorial office is at Üllői-út 26, Budapest VIII; the annual subscription varies, being 60 florins for those who own a pharmacy, 36 florins for employed pharmacists; and 18 florins for university employees and university students.

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On entering its 10th year of publication, *Medicina del deporte y del trabajo* (Buenos Aires, vol. 10, no. 40, May 1946), restates its aim to study scientifically the special problems arising from sport and work and to consider methods and legislation for dealing with them. The editor expresses satisfaction with the tremendous advances made during the last ten years in the provision of safer and more healthy conditions and better medical services for workers in industry and for members of sports-organizations. This number contains original articles on the study of movement, the medical and social problems involved in cases of disability or illness arising from work or sport, their causes, prevention and legal implications. In addition, the journal contains the text of the resolutions reached by the second convention of doctors especially concerned with industry, held in November and December 1945 in Buenos Aires, and the text of the resolutions of the third south-american congress of doctors connected with sports organizations. A further section contains bibliographical notes and comments.

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From Buenos Aires come two other journals. The first, *Boletín de la Asociación Odontológica Argentina*, is the official organ of the Asociación Odontológica Argentina. An editorial in this number (vol. 17, no. 199, January 1947) stresses the need for dentists to keep in touch with new methods and materials in dentistry and contains an account of a study-tour of the USA recently undertaken by members of the Asociación. A further section gives a list of the names of newly-elected officials of similar organizations throughout South America.

The second of these journals, *Index de neurologia y psiquiatria*, is published under the direction of Dr. Roque Orlando of the department of neuropsychiatry and the malarial-therapy centre of the Hospicio de las Mercedes, Buenos Aires. The number received (vol. 6, no. 7) consists of a single review-article and a short book-review section. The article, by Drs. Roque Orlando & Maximo Arndt, is on penicillin in general paralysis; after brief reference to the literature on penicillin in general, and surveying in more detail the work done on penicillin treatment of neurosyphilis, the authors give a fairly detailed report of their own experience of 57 cases of general paralysis treated with penicillin at their hospital.

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Latin America is also represented by three other journals—brazilian, cuban, and mexican. In the first number of *Revista do Hospital das Clinicas* (São Paulo, vol. 1, no. 1, January 1946), the official organ of the Hospital das Clínicas of the Faculty of Medicine of the University of São Paulo, the editors express confidence that it will make the work of the Hospital das Clínicas more widely known in Brazil and in other countries, and they affirm that a very high standard will be maintained in the articles chosen for publication. Selection will be made by professors of the Faculty of Medicine. This number contains 112 pages, comprising 8 original articles and a section giving notes of medical meetings held at the hospital. The journal will be published quarterly.

Anales de la Academia de Ciencias Médicas, Físicas y Naturales de la Habana, (vol. 84, no. 1), commemorates the 84th anniversary of the foundation of the Academy and contains the text of the presidential address delivered by Dr. Jose A. Presno at the commemorative session held in May 1945. The text of an address by Dr. Raimundo de Castro y Bachiller given on the same occasion is also included. This address gives an account of the Academy's activities during the academic year 1945-46, and the journal also contains the text of a discourse by Dr. Angel Arturo Aballi on the child and the future of humanity, in which he stresses the need to provide a good environment and adequate social services for mothers and children.

In the first number of *Aisa* (vol. 1, no. 1, September 1946), the editor states that the object in launching it is to further the cause of medical education in Mexico, to help its citizens to co-operate individually in helping to improve the nation's health and standard of living, and to provide members of the medical profession with a medium for the expression of opinions and theories. This number contains seventeen original articles on a variety of subjects, including the campaign against tuberculosis with special reference to Mexico, problems of radiographical technique, and ascorbic acid and haemotherapy in the treatment of pertussis. There is also a section of abstracts from foreign journals.

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Symptomatic of intensification of interest in biophysics is the new french journal, *Atomes et Radiations*, published by Expansion Scientifique Française, which deals with physics, biology and medicine. The present number (vol. 1, no. 6) consists of two original articles—of which one, by Lacassagne, on " The influence of wave-lengths on certain lesions produced by the irradiation of mice " is the french version of a paper read to the Section of Radiology of the Royal Society of Medicine in March 1946—a report on the work done in Chicago on plutonium, an abstract-section, and a short book-review section.

Strasbourg, one of the most vigorous of french medical centres, provides *Strasbourg Médical*, which appears three times monthly, and is published under the general editorship of Dr. Paul-Emile Arbinet la Bessède, with the aid of an editorial committee of professors drawn from the medical faculties of Strasbourg, Lille, Besançon and Luxembourg. The present number (1947, vol. 107, no. 3, 25 January) comprises the following sections : a comment on current affairs consisting of a list of german doctors accused of war-crimes; a section of original articles; notices of new books; and a short section containing items of news about personalities. The original-article section includes a review of foreign work, published since 1942, on neurology and psychiatry, by M. Schachter of Marseilles, who refers to the *Neurology* number of *BMB* (vol. 3, no. 1) and also to an article in the *Physics in Medicine* number (vol. 3, no. 3) by A. H. S. Holbourn on " The mechanics of brain injuries ".

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In an editorial note to the reader of no. 6 of vol. 2 of *Cahiers Médicaux de l'Union Française*, J.-M. Montpellier, of Algiers, outlines the two-fold purpose of this journal: to establish direct contacts in the field of medicine and public health between the various units of the french overseas empire, and to keep the mother-country informed of the activities of her pioneer outposts. In addition to original articles, the journal includes reports of societies; reviews of books, journals and theses; a section containing local medical faculty and hospital news; and a section of comment and correspondence. Finally, there is an inset supplement on therapeutic questions; the one in the present number is on the treatment of burns. The original-article section in this number consists of six clinical articles based on the experience of the authors in various parts of the french empire, and one long review-article on avitaminosis and pregnancy.

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The title of *Archivio " E. Maragliano " di patologia e clinica* (Genova, vol. 1, no. 1-2, January-April 1946), is a gesture of homage to the memory of Dr. Edoardo Maragliano, who devoted more than 40 years of his life to work at the Clinica Medica di Genova. The journal is published at two-monthly intervals and is composed of two sections, one containing articles on scientific subjects and the other articles on clinical subjects. The present number contains three articles in each section with summaries in French, Italian, German and English.

Also from Italy is *Folia cardiologica* (Milano, vol. 5, no. 1, February 1946), official organ of the Gruppo Cardiologico Italiano, which is published at two-monthly intervals. It contains original articles only on subjects relating to the circulatory system. The present number comprises six articles, the first of which deals with the electrocardiogram in the prognosis of myocardial infarct by Dr. Guiseppe Frau. Further articles deal with the mechanism of ventricular fibrillation by Dr. Aldo Selvini, the circulatory system in exanthematous typhus by Dr. Arrigo Poppi, cardiological observations in obesity by Dr. Salvatore de Renzi, a study of the electrocardiogram in hyperthyroidism by M. Cellini and A. Selvini, and of rheumatic infection in the etiology of paroxysmal tachycardia by Giuseppe Frau.

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Anales del Ateneo Médico Leonés (Ordoño, Leon), the official organ of the Ateneo Médico Leonés, is published under the direction of its president, Dr. Enrique Salgado. Number 7 of volume 3 consists of 23 pages and contains two original articles, the first of which, by Dr. Joaquin Garcia Morán of the Hospital Provincial, Oviedo, discusses the treatment of cancer of the stomach. The second article, by Dr. J. Alix of Madrid University, makes a comparative study of the advantages of temporary and permanent collapse in collapse-therapy of pulmonary tuberculosis. The journal also contains a reprint of an article in *Medicina Española* by Dr. F. Martinez on the diagnosis of moles, and there is a section containing abstracts from spanish and foreign journals.

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According to the publisher, the Washington Institute of Medicine, the *Quarterly Review of Medicine*, an abstract-journal now in its 4th volume, is ambitiously intended " to keep physicians informed as to current discoveries and advances in internal medicine with a minimum of expenditure of time and effort." Internal medicine is used in the broadest sense to include cardiology and gastroenterology, infectious diseases and chemotherapy of infectious diseases. A few abstracts from the best-known and most-accessible foreign journals are included, but as the majority are american, the journal is of most interest to those needing access to the medical literature of that country. A useful addition is the inclusion in the heading of the author's official address.

Historical Notes

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SOME NOTES ON THE HISTORY OF LACTATION

At the beginning of the eleventh century A.D. the persian physician Avicenna, in the first book of his *Canon of medicine*, set down certain points in connexion with the feeding of infants.[1]

"Whenever possible, the mother's milk should be given and by suckling. For that is the aliment of all others most like in substance to the nutrient material which the infant received while in the womb—the menstrual nutrients of the mother. It is these which are changed into milk after parturition, and such milk is better adapted for the infant. . . . If there be anything to prevent the mother from giving milk to the babe—for instance, owing to her weakness or to the defective quality of her milk, or because it runs too quickly, a wet-nurse should be selected."

This selection needed great care. The woman ought to be between twenty-five and thirty-five years old, of medium build, with a good colour, strong-necked and broad-chested, the breasts firm, the nipples well-formed but not too large. Her character and personal habits must be good, her nature equable and "slowly aroused by the bad passions of the mind such as anger, gloom, fear, etc. For all these injure the constitution and may change the milk or pass into it, or even prevent its secretion. It is for this reason that some people reject a nurse who is stupid." Nor should the wet-nurse permit sexual intercourse,

"for this disturbs the menstrual blood and diminishes the quantity of milk and alters its composition. . . . Moreover she might become pregnant, in which case there would be a dual unpropitious influence—to the wet-nurse herself in that whatever is attenuated in the blood enters into the nutriment of the embryo, and to the embryo in that it loses as much from the mother's aliment as passes on to form milk".

The milk itself should be in consistence

"between coarse and fine; the colour white . . . the odour good, without acridity or pungency; the taste sweetish. . . . The quantity should be of a certain amount. It must be homogeneous. . . . The consistence may be tested by allowing the milk to run over the finger-nail. If it flows easily, it is thin; if it does not flow over the inclined nail, it is thick. Again, place some in a glass vessel, and drop a little myrrh into it, and stir the two together. The aquosity and the degree of caseity are then evident. The milk is laudable and attempered if the watery part and cheesy part are equal".

The wet-nurse appointed to feed a newly-born child should herself have given birth in every way normally, between six and eight weeks previously.

In general, the health of the nursing woman should be maintained by a plain nutritive diet, by moderate exercise, by sufficient sleep, and if necessary by medicines. For the surest way of controlling the health of the child was by controlling the quality of the milk it sucked.

The child need not be suckled on the first day of life, save in exceptional circumstances and then preferably by someone other than the mother, but might be put to the breast so soon as the mother had sufficiently recovered from the ordeal of giving birth. It was to be fed "twice or thrice in the day at first, and it should not be allowed to take too much." Avicenna advised drawing off a little milk from the breast before each feed "to encourage and facilitate its flow." The nipples might be anointed with honey.

Most of the rules thus laid down by Avicenna—particularly those relating to the choosing of a wet-nurse, to the qualities desirable in the milk itself, and to the duration of lactation—continued to be observed with little modification for many centuries. They are repeated, for example, in Paulo Bagellardo's *De infantium aegritudinibus* (Pavia, 1472), the first printed book to deal solely with the rearing of young children; and in the almost contemporary monograph by Bartholomäus Metlinger, *Ein Regiment der Jungen Kinder* (1474).

By the eighteenth century the employment of wet-nurses was perhaps more common than it had ever been before, and the baby-farms which relieved these women of the care of their own offspring were in their notorious heyday. Yet the practice of rearing the child on milk or pap from a perforated cow-horn, pap-spoon or boat was growing. This trend in infant-feeding was confirmed towards the end of the century, by the introduction of the conical glass feeding-bottle, its tubular mouthpiece enclosed in an overlapping finger of linen, parchment or wash-leather.[2]

Michael Underwood (1737-1820), the London obstetrician, who was among both the first and the last to hold the licence of the Royal College of Physicians to practise midwifery, especially praised the glass feeding-pot. It is, he wrote,

"so contrived, not only as to please the child by its resemblance to the nipple, and the milk coming slowly into its mouth; but also to afford the infant some little degree of labour, in order to acquire the quantity it needs, which the horn does not; by which means the food is also duly mixed with saliva".

He directed that the pot should be very carefully cleansed and scalded "at least once every day."

As to the food itself, in hand-feeding, Underwood recommended the milk of cows, or in some cases asses, to which

"should be added a little thin gruel, or barley-water. . . . A few weeks after birth, and I think in general the sooner the better, instead of the barley-water or gruel, there should be mixed with the milk a small quantity of a light jelly made from hartshorn shavings. . . . The design of the jelly is obvious and rational . . . the milk of quadrupeds . . . is produced from vegetable juices only, whilst breast milk is formed by a mixture of animal and vegetable food. A little Lisbon sugar may be added. . . . At first the milk ought to be boiled, to render it less opening; but, when the child is several months old, or may chance to be costive, the milk need only be warmed".

Underwood at the same time was emphatic that "every child should be suckled, and always by its own mother, where her health can safely admit of it." At this point, Samuel Merriman, editor of the eighth edition (1826) of Underwood's *Treatise on the diseases of children*, added a footnote:

"I am convinced that the attempt to bring up children by hand proves fatal, *in London*, to at least seven out of eight . . . and this happens, whether the child has never taken the breast at all, or having been suckled for three or four weeks only, is then weaned. *In the country*, the mortality among dry nursed children is not quite so great as in London, but it is abundantly greater than is generally imagined."

On the subject of weaning, Underwood expressed what was the orthodox opinion at the end of the eighteenth and beginning of the nineteenth centuries:

"A child ought to be in good health, especially in regard to its bowels; and ought first to have cut, at least, four of its teeth, unless that process should commence very unusually late. This seldom takes place till the child is near a twelvemonth old; and it may be observed that healthy women, who suckle their own children, and take proper exercise, do not usually become pregnant again in less time, and this, I conceive, may be considered as one intimation of the properest period. . . . Any preparation for weaning is generally needless. . . . I have lived, as it were, in the nursery for many years, and never found any ill effects from the sudden transition from breast-milk to artificial food when properly chosen."[3]

By the middle of the nineteenth century, informed opinion on the duration of lactation had undergone a further change. In 1848, A. Peddie, physician to the Minto House Hospital and Dispensary in Edinburgh, wrote:

"I should say almost invariably at the conclusion of one year from the birth of the child, the secretion is found colostric even in the healthiest women. To this I have met with no exception; and, seeing that such is the case, I believe that lactation continued beyond the ninth month is decidedly improper. . . . Mothers, however, are often found continuing the child at the breast from personal considerations, without particular reference to its wants. What I allude to is, the supposition that during nursing protection is afforded against the occurrence of a new pregnancy. This idea, I think, is an erroneous one; and it is to be regretted that medical men have not set themselves more against the practice founded upon it."

He added:

"when a woman becomes pregnant during lactation, the microscope is a most important diagnostic guide; for then the colostric characters of the milk are apparent, and thus we can, without hesitation, advise an immediate abandonment of suckling."[4]

The subject of lactation in the second half of the nineteenth century seems to be chiefly remarkable for the ingenuity of the feeding-bottles invented and the variety of proprietary baby-foods placed on the market.[5]

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B. M. Duncum

1142

THE STORY OF ARTIFICIAL INFANT-FEEDING

The scientific study of infant-nutrition is a modern development, the success of which can easily be demonstrated by comparing the health of the infant-population of today with that of 1847. But it would be a mistake to suppose that people of an earlier age were not aware of the problems which modern knowledge and equipment have enabled us to solve. It is just over a hundred years since the first proprietary baby-foods were placed on the market, but from the time of Soranus of Ephesus (fl. 100 A.D.), author of the oldest work extant on pediatrics, efforts were made to provide a substitute diet when it was impossible for the mother to feed her own child. Soranus confined himself to the choice of a good wet-nurse, judging the quality of the milk by the "finger-nail" test[1] which was still recommended by Smellie in 1752.

The fact that Soranus does not mention artificial foods, either as a supplementary, or as a completely-substitute diet, does not mean that such were unknown to the Romans, for there survive children's feeding-vessels, in terra-cotta, clay and even glass, some almost identical in shape with the modern version, from as early as the second or third centuries A.D. That the use of such vessels[2] was not confined to the Romans is shown by a thirteenth-century illuminated manuscript with an illustration of a woman feeding an infant in her arms by means of a horn, and a poem on the care of the body, written by Heinrich von Louffenburg in 1429, was printed in 1491, 1532, 1544, and 1549 with woodcut illustrations, one of which shows a child feeding from a "bottle" rather similar in shape to that of some of the roman clay vessels.

The first clear indication which we have of the kind of food given to children from these vessels is given in an excellent chapter on infant-feeding contained in Simon de Vallambart's *Cinq livres* (1565), the first french book on children's diseases. He there declares that it is customary to give other foods, in addition to breast-milk, from the age of three months or even earlier. (Paré thought it permissible from 10 or 12 days.) As a basis for such foods, he suggests cow's milk or goat's milk (which he thinks preferable) boiled with semolina or flour or white breadcrumbs, or sometimes with the yolk of egg. He condemns as a source of disease the practice of nurses who chew the food before placing it in the child's mouth, and he describes a feeding-vessel in the shape of a horn, with the narrow end shaped like a teat. Evidence from other sources proves that artificial feeding was by no means uncommon in sixteenth-century France. Among the Paris street-cries recorded in 1545 is one of "Milk for the babies", and Henri IV himself was reared on ass-milk.

The common belief that undesirable moral qualities of the wet-nurse could be conveyed to the infant by her milk may have had something to do with the adoption of alternative foods to breast-milk. One suspects that this fable may have originated in a dreadful warning given by a skilful physician to some matron who was reluctant to nurse her own child but, whatever its origin, physicians continued to make good use of it throughout the centuries, and it was repeated by Michael Ettmüller, Jean Astruc and Struve as late as the eighteenth century. This was the century which saw the beginnings of the infant-welfare movement and the establishment of foundling hospitals, which gave for the first time to physicians a controlled field of inquiry into the care of infants in health and disease. William Cadogan's classic *Essay upon nursing, and the management of children* (1748) was one of the first-fruits of this movement. His sensible and enlightened advice includes suggestions for feeding—"thin light Broths. with a little Bread or Rice boiled in them ; . . . a little Bread and Water boil'd almost dry, and then mixed with fresh Milk not boiled . . . for boiling alters the Taste and Property of it."

In 1760 the french physician J. C. Desessartz published his *Traité de l'education corporelle des enfans en bas age*, in which he attempted to table the comparative values of different kinds of milk, basing his judgment on chemical characteristics. He placed human milk first because of its low caseous content and the softness of its curd, and that of the ass and mare, the goat, the cow and the ewe followed in that order. He also mentioned malted food. In the following year Thomas Young presented a graduation thesis at Edinburgh which reported some pioneer work into the chemistry of milk based on actual experiments, and in 1762 John Rutty brought out his *Analysis of milk and the several species thereof*. Hugh Smith, in his *Letters to married women* (1772) asserted his preference for "cow's milk to every other kind of nourishment in the early months where it is necessary to bring a child up by hand; . . . the milk of cows appears, I think, to be the properest substitute we can make for that of the breast; and will answer best after the first month or two without boiling." In the last year of the century, the third volume of the fourth edition of Michael Underwood's well-known work appeared with valuable new observations on infant-feeding, and a table (quoted from Boysson) showed the analysis of the various kinds of milk. He strongly condemned the use of "pap" (bread and water), and held that milk, preferably cow's milk, was the most proper food for infants, but that it should be boiled. Other interesting points were his recommendations of rice, tapioca and barley-water.

Die Mutter.
Ich wil mein Kindlin ſetzen ab/
Sein pflegen wol als ich vermag.
Vom letzten ſag ich dir furwar/
Wenn nu das Kindt ins zweyt jar/
Der Frawen brüſt haſt wol geſogen/
So ſoln ſie im denn werdn entzogen.
Jedoch nit all zu ſchwind zu gehe/
Mit zarter ſpeis daſſelb geſchehe.
Von Zucker linden trünckelein/
Sol man im ſtetigs geben ein.
Auch ſpeis die ſich dawet leichte/
Wo aber ſolchs nicht geſchichte/
Vnd gibſt im ſpeis von grober koſt/
Keins dings du denn gewiſſer haſt/
Denn das im daruon wechſt der Stein/
Der Krampff/in henden/füſſen vnd bein.
Mgn ſol im doch in heiſſen tagen/

Wellcome Historical Medical Museum

Woodcut illustration to poem by Heinrich von Louffenburg, in the *Regiment der Gesundtheit* (1549)

With all this renewed attention to infant-feeding came a revived interest in the feeding "bottle". George Armstrong, in 1777, advocated a horn, with the finger of a glove fixed on the narrow end as a teat, and in this he was warmly supported by Heberden. Hugh Smith offered to the public his well-known "bubby-pot", and various other kinds of pewter vessel were in common use, all with some kind of teat made from linen, parchment or leather over a small sponge. Struve (1798) condemned the use of pewter, and recommended a glass bottle with a short neck and a perforated cork, and stressed the great importance of keeping such vessels scrupulously clean.

It is impossible to say how strictly the advice of all these physicians was observed, but the mortality figures in the foundling hospitals (Paris, 80 % ; Dublin, 99 %) at the end of the eighteenth

[1] [For a description of this test, see article (*BMB* 1141) in this number by B. M. Duncum.—Ed.]

[2] [See also article (*BMB* 1143) in this number on ancient feeding-bottles by F. Tubbs.—Ed.]

century show that something was seriously amiss with the care of infants as it was actually carried out in practice. In the early nineteenth century, according to Marshall Hall, "seven in every ten children brought up by hand" died. It is little wonder that, with such figures, good physicians continued to impress upon mothers the fact that nothing could safely replace breast-milk in the first year of life. Nevertheless, the changes in society resulting from the industrial revolution, the growth of cities, the increasing employment of women and the growing number of institutions devoted to children, all gave additional incentive to the search for a satisfactory infant-food. By 1840, the earliest proprietary foods were on the market, the first being the fashionable "tops-and-bottoms" (rusks) of Messrs. Robb & Co., closely followed by Hard's Farinaceous Food and Lemmon's Biscuit Powder, while in 1867 Justus Liebig introduced his well-known "malted food". Being in liquid form, this was soon ousted by preparations of concentrated and dried cow's milk. with or without other ingredients, in the safe and convenient form which we know today.

In 1884 Eustace Smith asserted that "The successful rearing of an infant by artificial means is not a difficult matter". At that time, this probably held true only of a physician or an exceptionally intelligent parent. Today, thanks to the great strides made in the science of nutrition, with its experimental research into essential food-factors, many excellent patent foods provide a complete diet for the young infant, while the spread of education, the establishment of child-welfare clinics and the day-to-day guidance which parents can obtain in them, have made Smith's words true of the population in general.

F. N. L. Poynter

1143

ROMAN INFANT-FEEDING-BOTTLES WITH PARTICULAR REFERENCE TO ROMANO-BRITISH AND BRITISH MEDIEVAL VESSELS

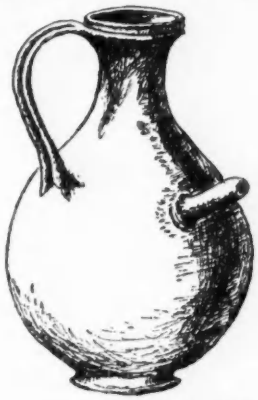
The subject of infant-feeding-bottles in earliest times belongs to the field of archaeology. Ancient writers do not mention them, but some antiquaries have claimed that certain greek vases circa 700 B.C.–500 B.C. (in the British Museum) are prototypes of roman feeding-bottles (Cuming, 1870). Dr. Sambon of Rome was also of the opinion that some roman feeding-bottles can be assigned to an early date, "perhaps the fifth or sixth centuries, B.C." (Sambon, 1909). The positive identification of certain roman vessels as feeding-bottles is due to ancient burial rites. Pliny wrote, to quote a translation by an english doctor, Philemon Holland (1635): "It is not the custome in any countrey to burne in a funerall fire the dead corps of any infant before his teeth be come up". This statement is supported as far as Britain is concerned by the bodies of babies sometimes found buried on romano-british villa sites, and child-graves.

It is to this practice of inhumation mentioned by Pliny, together with the provision of food and grave-furniture for the use of the dead, that posterity owes the recognition of early feeding-bottles. For certain small vessels now called tetinae, and once thought to have been oil-cruses for filling lamps, have been found in the graves of very young infants in place of the usual food-offerings. When it was noticed that the children had died "during the period of lactation" (Sambon, 1909), and the small bore of the sucking tubes of the vessels considered, the purpose of these was plain.

Feeding-bottles in the Western Roman Empire were usually made in terracotta of varying texture and colour, but an example executed in glass has been found in Paris (Sadler, 1909). A very small feeding-bottle made of lead is on record, but this was obviously of no practical value, and was probably intended as a votive offering (Sambon, 1909). The simplest type of roman feeding-bottle consisted of a conventional bulbous clay vessel possessing a wide opening at the top, but with an appendage in the shape of a spout of unusually small bore. An example found in Germany was about 7 cm. in height and of a fawnish colour (Cuming, 1870). A specimen found in Kent in 1848 (Crafter, 1848-9) and another presumably in the possession of the Wellcome Foundation may also belong to this class. Unfortunately the Wellcome Museum's infant feeding-bottles are packed away so that it has been impossible to identify their early bottle with certainty, but a photograph has been published (Still, 1931).

The second type of feeding-bottle was a taller, rather more elaborate version of the first. This was the commonest type and apparently persisted into Elizabethan times. The second roman type was some 10 cm. in height, with a narrower, slenderer neck than the first type, and possessed a handle placed at right-angles to the spout. An example found near Cologne was of fawn-coloured terracotta with the upper half shaded a deep chocolate-brown, but the romano-british specimens which have been found are of either a reddish or greyish colour. The fine example illustrated in fig. 1 was found on the site of Smithfield Market, London, on 2 November, 1865. It was some 11 cm. in height with a reeded handle so placed that the vessel could be held in the left hand.

FIG. 1. ROMANO-BRITISH FEEDING-BOTTLE



(F. Tubbs, after H. S. Cuming)

The third type of roman feeding-bottle was far moreel aborate than either of its predecessors. Shaped like a human breast, it retained the handle at right-angles to the feeding-tube as in the second type. This third type was filled from the bottom by means of an internal tube running almost to the top of the vessel. Built on the "unspillable inkpot" principle, this vessel retained its contents uncontaminated by flies or insects, and the milk could be drawn out only through the feeding-tube (Sadler, 1909). An example illustrated in Still's work (1931) with the legend "Baby-feeder in terracotta: roman" appears to be of this type.

A few other shapes that do not belong to the main line of development were also employed; some were shaped like goat-skins, others like animals, but all possessed the feeding-tube that was distinctive of this type of vessel. One boat-shaped example (Still, 1931) has been found which suggests the shape of feeding-bottle now in use, but the date of this specimen is uncertain.

The medieval british feeding-bottle bore a striking resemblance to the infant feeding-bottle used in roman Britain and referred to in this note as the "second type". Like its predecessor it possessed a sucking-tube at right-angles to the handle, though the shape of the vessel itself approximated to that of the medieval jug. An example found where the Temple shore ran down to the Thames in London was discovered in 1864. It was made of earthenware and coloured with a dull greenish glaze. Nearly 10 cm. in height, it measured rather more in diameter than the Elizabethan specimen illustrated in fig. 2, which was slenderer though of the same height. This specimen was chosen for illustration here because it bears comparison with fig. 1, and like the romano-british specimen, was also found in London. The Elizabethan bottle had a yellow glaze, and was found in Old Swan Lane, Upper Thames Street, during September 1867 (Cuming, 1870).

It is not suggested that there is a direct line of descent from the romano-british to the Elizabethan feeding-bottle. The gap was probably bridged by the baby-feeder made from cow's horn depicted in the thirteenth-century miniature in the Wellcome Museum (Still, 1931). The horn was still used in the latter half of the eighteenth century (Drake, 1930).

In conclusion, a brief allusion will be made to teats. It is obvious that some form of teat must have been used with the romano-british and medieval feeding-bottles, especially as some specimens were made of absorbent pottery that would cause the

FIG. 2. ELIZABETHAN FEEDING-BOTTLE

(F. Tubbs, after H. S. Cuming)

lips to adhere to the feeding-bottle if no protection was afforded. There is little doubt that the teat from a very young calf was employed, as in later times until the period when teats were first manufactured. In the eighteenth century two pieces of parchment were sewn together to make a teat, and from the nature of the material used this might well have been a survival from a much earlier period. It has been suggested (Cuming, 1870) that the Victorian practice of some country nurses, of drawing the finger of an old kid glove over the spout of a teapot used as an infant feeding-bottle, was an echo of the time when the teat of a calf was used with a feeding-bottle by our ancestors. The first teats to be made specially for infant-feeding bottles were large and rather cumbersome (Sadler, 1909), and obviously inspired by the animal teats employed for centuries, but even the shape of artificial teats has been modified by modern manufacturers, so that there is now little about the modern feeding-bottle that is reminiscent of the types of two thousand years ago.

F. Tubbs

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1144

A SPANISH EPIDEMIC OF PLAGUE IN THE SIXTEENTH CENTURY

In a small book[1], Dr. Don Jose Viñes Ibarrola gives an account of an outbreak of bubonic plague during August-November 1599, in Pamplona, the chief town of spanish Navarra. The main features of the outbreak can be stated in a few words and the interest of this book lies in the fact that original contemporary documents are referred to and quoted. The town had been repeatedly visited by plague, and each time this occurred vows were made, but it was a case of " When the Devil got well, the devil a saint was he " and the vows were forgotten.

In November 1596, the disease was rife in Flanders and spread thence to various parts of Spain, and it is thought that Pamplona was infected by clothes and effects brought by ship from Dunkirk. Towards the end of 1599, women came from the french Navarre (Basses Pyrénées) and Magdalena, a suburb of Pamplona, buying cloth and other things and a few days later some fell sick and died. This is said to have been the start of the outbreak. That the epidemic was less severe than it might have been is ascribed to the energy of the Bishop Don Antonio Zapata y Mendoza, who took a large part in the organization of preventive measures and kept up the spirits of the inhabitants. Guards were placed to prevent ingress to and egress from houses attacked ; passes were given to those allowed to enter the area, and all those going out from it to work had to have a pass and return by the same gate as that by which they went out. Visitors were appointed to see that so far as possible no cases were hidden or overlooked. If anyone died who had not been medically attended, he could not be buried until a doctor had examined the body to see whether there were any buboes or other signs of plague, and if such were found, all in the house were quarantined.

The doctors concerned with the outbreak, and whose records and reports are given, are named, among them Joan de Lortia who, it is said, devoted 42 years of his life to the organization of anti-plague measures in various parts of France and Spain. The measures undertaken included, in addition to what has been stated above, isolation of patients and contacts, cleanliness of houses and household-goods, disinfection of houses, clothes, etc., all of which, it is now well known, would help in elimination of fleas, though the aims in view then were to avoid direct contact between the sick or possibly sick and the healthy, as the breath was believed to carry infection ; the selling or giving away of clothes was forbidden and all washing of clothes had to be done at home. A hospital was established outside the infected area, staffed by doctors, an apothecary, nurses, guards and grave-diggers ; there were special kitchens and cooks appointed to prepare the food.

How successful these measures were can be seen by comparing the figures of an outbreak in Santander nearby in 1596 with those of the Pamplona outbreak.

	Population	Cases	Morbidity	Deaths	Fatality
Santander	1,500	689	45.93%	600	87.0%
Pamplona	30,000	344	1.14%	276	80.2%

Thus, though the fatality rates were nearly the same, the morbidity was 40 times as great in Santander. Little need be said regarding the treatment of patients. Burning of aromatic woods in the rooms was advocated, and the taking of " plague tablets," one three times a day after a prayer to the Almighty for preservation from sickness. Laudanum, sandalwood, amber, musk were others in a long list of remedies. An interesting account.

H. Harold Scott

[1] [For particulars see *Book Reviews.*]

1145

THE RENAISSANCE AND ENGLISH MEDICINE

In the recently-published[1] Thomas Vicary Lecture for 1945, Sir Arthur MacNalty remarks that it was not until the value of greek thought was manifest to the practical Englishman that the influence of the Renaissance became widespread. Thomas Linacre, one of those who brought the new learning to Oxford, was instrumental in establishing, in 1518, the Royal College of Physicians, a body empowered to control the practice of medicine in and around the City of London.

As is shown in the famous Holbein painting, Thomas Vicary in 1540 received from the hands of Henry VIII the Act of Union between the Barbers and the Surgeons, and the new body thus formed regulated the practice of surgery in the London area.

Thus were the twin professions of Medicine and Surgery consolidated and regulated in Tudor times. Sir Arthur MacNalty enables his readers to visualize the conditions of life in England at that day by his clear sketch of the Tudor background. At the time of the Armada the population of England was under five millions. Wages were high and food was cheap, so that the spanish nobles were amazed to find that the common folk fared as well as the king. The standard of nutrition was good—more people died of over-eating than of under-nourishment. Dress was costly and ostentatious, and the style of architecture was solid and ornate. That some attention was paid to public health was evident in the improvements in water-supplies and the regulations regarding disposal of sewage. The new learning spread from the Universities to the grammar schools, where boys were taught to read, write, and speak latin. " On the whole, there was less illiteracy among the people of England in the sixteenth century than in the first half of the nineteenth."

[1] [For particulars see *Book Reviews.*]

In spite of this apparent wave of prosperity there was much disease in England in Thomas Vicary's days. Although the incidence of leprosy had become reduced, syphilis was a deadly scourge. Tuberculosis was prevalent and there was much malaria. The "hot agues" appear to have been typhus, a disease frequent in the towns and in overcrowded gaols. But the deadliest epidemics of Tudor times were bubonic plague and the "sweating sickness". Plague had remained endemic since the year of the Black Death, which had destroyed half the population of England. The worst epidemic of the century was in 1563-4. Flight from the infected area was the chief protective measure, but there were many regulations regarding sanitation and scavenging. The sweating sickness took the form of a succession of epidemics between 1485 when Henry VII landed at Milford Haven, and 1551, when the final outbreak occurred, and was described by Dr. John Caius in *A Boke or Conseil against the . . . Sweating Sickness.* The only modern malady which bears any resemblance to sweating sickness is miliary fever, "the Picardy sweat", of which there were many epidemics on the Continent, though not in Britain, between 1718 and 1906 or even later.

The Tudor physicians could do little to check the prevalent epidemics, but a few outstanding pioneers introduced reforms and improved the public health. Prominent among them was Sir Thomas More, 1478-1535, Speaker of the House of Commons, Lord Chancellor, humanist and health reformer, saint and martyr. The citizens of his *Utopia* (printed in 1516) esteemed health as the greatest of all pleasures. More's comprehensive programme of social medicine included a public water-supply, drainage, and cleansing, public hospitals for rich and poor alike and isolation-hospitals for infectious disease, communal meals, nursery schools, free education, eugenic mating—in brief, many of the aspirations of today. Appointed to take charge of health-measures, More pleaded with Henry VIII to spare the hospitals while pursuing his scheme for destroying the monasteries. But the king was bent on wholesale suppression and destruction. He ignored the advice and a few years later, in 1535, he sent poor Sir Thomas to the scaffold—"the blackest crime ever perpetrated in England under the form of law". It was only through the public-spirited action of the Corporation of London that five Royal Hospitals were preserved, and Henry was already on his deathbed when he agreed to pose as their first founder. If Sir Thomas More's enlightened policy had been followed, England would not have been obliged to wait for three hundred years for the initiation of national public health.

Another social reformer of Tudor times was Sir Thomas Elyot, whose *Castel of health* (1534) was widely read, while a third pioneer was the quaint Dr. Andrew Boorde, whose *Breviarie* and *Dyetary* are full of sound commonsense and shed a light on the social structure of that day.

Sir Arthur MacNalty also refers in this lecture to the revival of surgery under Thomas Vicary, and his successors Thomas Gale and William Clowes. We do well to honour such men, who made possible the discovery of William Harvey, the investigations of John Hunter, and the triumphs of present-day medical research.

Douglas Guthrie

1146

DOCTORS DIFFER

The terse proverb, "Doctors differ", is a fundamental truth of medical practice. Commenting upon the seven spectators gathered around the teacher, Dr. Nicholaas Tulp, in Rembrandt's well known "Lesson in Anatomy", Dr. Harley Williams remarks[1] that to each of those young surgical apprentices the lesson has conveyed a different meaning. All are filled with the same passionate curiosity, yet it appears in seven versions. It is right that doctors should differ, and it would be a sad day for the sick if their advisers were obliged to maintain uniformity in their outlook. Each good doctor is an individualist, and for each the way is different. From this most appropriate introduction the author proceeds to sketch the careers of five medical pioneers who dared to differ from their contemporaries and thus inaugurated new epochs in various branches of medicine: John Elliotson in psychological medicine, Hugh Owen Thomas in orthopaedics, James Mackenzie in cardiology, William Macewen in neuro-surgery, and Robert William Philip in tuberculosis.

The strange career of John Elliotson occupies about one third of the book. It is a neglected, yet significant, chapter in the history of medicine. Elliotson was a popular professor of medicine at University College, London, and in the front rank as a consulting physician, when he first espoused the cause of Mesmerism, or Animal Magnetism, as it was called.

His colleagues on the medical staff of the hospital were not impressed by what appeared to them to be an unwarranted departure from the recognized methods. Nevertheless the newly-established weekly journal, *The Lancet*, devoted many pages to full reports of Elliotson's lectures and experiments. Thomas Wakley, the editor, was fearless and progressive, and he wielded a powerful pen. His medical journalism showed no restraint, and led to a succession of lawsuits which merely strengthened his position.

With such strong support, it appeared for a time as though Elliotson might win his fight for recognition and establish a new branch of medicine. In the end, however, colleagues, Liston, Sharpey and others, demanded his resignation, while *The Lancet* withdrew its support and turned against him.

The materialism of the nineteenth century, with its excessive absorption in the physical body, could find no place for psychiatry in medical practice. John Elliotson was obliged to accept defeat, in a world not yet ready for his views. Only today is he coming to be recognized as a pioneer, and the author has done well to place him in the forefront of the quintette of heroes.

Hugh Owen Thomas, the Liverpool bonesetter's son, who introduced the methods of his father into regular practice and who passed on the torch of learning to his nephew, Robert Jones, may be regarded as the founder of orthopaedic surgery in Britain. His curious coat and peaked cap, his chain-smoking of cigarettes which he rolled himself long before the cigarette habit became universal, his breakfast of tea and bananas, his love of music and especially of the "Dead March in Saul," stamped him as no ordinary character. But there was no eccentricity in his simple and sensible dealings with the bones and joints of his patients. What the father did blindly and instinctively, the son did with reason and with a sound knowledge of anatomy. "His career is the standing refutation of standardized medicine," and although he wrote little and took no trouble to spread his doctrine, he built up the science of orthopaedics which was to be so brilliantly expounded by Sir Robert Jones.

Not very far from Liverpool stands the industrial town of Burnley, where a general practitioner, Dr. James Mackenzie, devoted the best years of his life to the study of the heart. The abnormal sounds, or "murmurs," and the irregularities of the pulse, such as missed beats, which had been regarded as dangerous omens, were all carefully studied by Mackenzie, who brought order out of chaos. He proved that sounds did not matter, and that many pulse irregularities were of no consequence, so long as the heart fulfilled its function. All this he did by devoting years of study to the records of heart- and pulse-movements traced upon smoked paper by an ingenious instrument of his own invention. He discovered what the heart could do and how far it might be trusted to fulfil its vital function. At the age of 53 he gave up his Lancashire practice and removed to London, where he rapidly achieved eminence. Alongside, and in contrast to, Sir James Mackenzie, the author places Sir William Osler, Professor of Medicine successively in three great centres, Philadelphia, Baltimore and Oxford. ". . . Osler was proud of what medicine had achieved, while Mackenzie was haunted by what medicine has still to learn, and . . . both philosophies are needed."

One of the most interesting chapters in this attractive book deals with the work of Sir William Macewen, with whose name is linked that of Sir Victor Horsley. A pupil and successor of Lister as Professor of Surgery in Glasgow, Macewen was a whole-hearted follower of the antiseptic technique which he applied to the surgery of bony deformities, and later, to brain-surgery. His wonderful successes in the treatment of brain-abscesses were set forth in his book on *Pyogenic diseases of the brain and spinal cord* which remains one of the classics of Surgery. Nor were Macewen's researches confined to surgery. He discovered fresh facts regarding the growth of antlers in deer, and he was a keen student of nature. Ever an individualist, he was certainly a doctor who differed from his contemporaries; he ". . . moved in his own orbit, by his own light," and rather prided himself on the fact that he was not a co-operator.

Sir Victor Horsley was another great pioneer of brain-surgery and a noted controversialist who held extreme views on Women's Suffrage and Total Abstinence when these subjects were the centres

[1] [In *Doctors differ*. For particulars see Book Reviews.]

of much debate. The author has clearly depicted his scientific achievements as well as his eccentricities.

The final chapter is devoted to the achievement of Sir Robert W. Philip in the fight against tuberculosis. Here Dr. Harley Williams speaks with authority, of his old teacher, in the field which he has made his own. Philip made fresh air a homely remedy, and not merely the prerogative of those who could seek its benefits in Switzerland or in the Black Forest. His Tuberculosis Dispensary, opened in Edinburgh in 1887, marked the beginning of a new era, a great experiment in social medicine. Philip evolved a scheme in which all the needs of the tuberculous patient were met, although in his day he was considered a rash enthusiast. A man of wide culture and a noted orator, he exercised a fascination over many generations of students. His methods have been adopted all over the world.

The american pioneer of open-air treatment for tuberculosis was one who was himself a victim and who found new life in the Adirondack wilderness. The sanatorium at Saranac Lake was the first of many such institutions in America.

In his admirable sketches of those differing doctors, Dr. Harley Williams has produced something more than a series of biographies. He has credited his five heroes with five separate philosophies, each one true. He has shown that there must always be an art, as well as a science, of medicine, and he has proved conclusively, in this delightful book which will fascinate many readers, that however widely doctors may differ, they will work with one object in view, the provision of health and the prevention of disease.

D. G.

1147

THE ROTUNDA HOSPITAL 1745–1945

In his recently-published history[1], Professor O'Donel Browne tells the story of the Rotunda Hospital, Dublin, from its foundation in 1745 by Bartholomew Mosse, up to 1945.

The book is divided into six sections. In the first two of these, the author describes the development of the hospital buildings and administration from a small beginning in a house in George's Lane. This was soon found to be inadequate and a new Dublin Lying-in Hospital was opened on the present site within 12 years. Reserved at first for maternity cases only, a gynaecological department was opened in 1835. Short biographies are also given of successive Masters.

The third section is devoted to an account of the age-long struggle against puerperal fever, in the treatment of which the Rotunda at times lagged sadly behind. The author rightly stresses the excellent work of Labatt and Collins. This section is extremely interesting and recounts the efforts made by various Masters to combat a deadly disease, the cause of which, before Holmes and Semmelweiss, Pasteur and Lister, was a mystery to them.

The fourth section gives an account of the progress of operative midwifery, including the use of the forceps, caesarean section, and destructive operations on the foetus. The author credits William Smellie with three caesarean sections performed for placenta praevia, but omits to state that these were carried out only after the death of the mother. Nearly one and a half centuries were to elapse before Lawson Tait was to stagger the obstetric world with a recommendation of caesarean section for placenta praevia.

The development of anaesthesia and gynaecology are described in the fifth section. The author falls into error here in recounting that delightful but wholly inaccurate story of how Sir Walter Scott advised Sir James Young Simpson that his coat-of-arms should be "a wee naked bairn" with the inscription "Does your mother know you're out?" Sir Walter Scott died in 1832. Simpson was knighted in 1866 (not 1870).

Eclampsia is the subject of discussion in the final section. As the author rightly claims, "the name of the Rotunda is inseparably linked with eclampsia because of the advances made there in its treatment". The name of Hastings Tweedy is forever associated with the problem of eclampsia, and his views and work are rightly given prominence.

The author considers Mosse, Ould, Clarke, Labatt, Collins, Macan, Smyly and Tweedy to have been the greatest Masters. Few will dispute his verdict.

[1] [For particulars see *Book Reviews.*]

The volume concludes with a chronological table of the main events in the Rotunda under each Master, plus a similar synopsis of the main events in Dublin and elsewhere in the obstetric world. There is also a graph showing the number of deliveries and death-rate during the 200 years.

At times, the author has not been able to resist the temptation to branch off into the history of obstetrics in general apart altogether from the history of the Rotunda Hospital. This is most pronounced in the section devoted to operative midwifery. To the keen student of obstetric history, this is probably no drawback, but one feels that, occasionally, the author is rather getting "away from the point". Nevertheless the story is a fascinating one, well told, and can be strongly recommended to all interested in the history of medicine and of obstetrics in particular. It may come as a surprise to learn that Irish Sweepstakes have not solved the financial problems of the Rotunda.

The book is beautifully produced and contains many handsome illustrations.

J. H. Young

Book Reviews

ANATOMICAL TERMINOLOGY

1148 Anatomical Terms: their Origin and Derivation

E. J. Field & R. J. Harrison. Cambridge, W. Heffer & Sons Ltd., 1947. vi + 165 pages. 17 × 10 cm. 7s. 6d. [£0.375]

This small book, excellent within its limits, ought to encourage the medical student to think about the anatomical terms he encounters. By discovering their meanings he will often be helped to understand structure and function in the processes they describe, and will acquire a taste for the history of anatomical discovery. The book will be equally useful to the professional anatomist. It is well produced, pleasing to handle and to read, and unlike most books of reference will fit easily into the pocket. The authors modestly define their purpose by a series of negatives: their book is not meant to be a medical dictionary nor an authoritative etymological treatise and will not "make up for the lack of a classical education". Yet it contains a quantity of useful instruction not easily findable in any other one source.

Drs. Field and Harrison assume in their readers a knowledge of the application of anatomical terms and concentrate on expounding derivations chiefly from greek or latin roots. This they do with care, stressing the evolution of meanings from a direct to an applied "lay" sense and thence to the anatomical meaning, often by analogy. This derivation is in many cases expanded by a discussion or criticism of the aptness of the term and a note on its earliest use in anatomy. For example the note on *fibula*, after giving the Latin original of "a pin or skewer" for fastening, hence a brooch, points out that Vesalius first used the word in anatomy, goes on to discuss *infibulation* by a silver needle and concludes: "Since all *fibulae* are thin and, in certain animals, often very narrow . . . and have sharp tips . . . it is probable that they were so-called from their resemblance to needles rather than brooches." Where the term includes the name of a discoverer they provide a thumbnail biography of the man thus commemorated by his "eponym". They do not try to give the precise references, which may be found in Dobson or Morton or other of the authorities to whom they refer, though occasionally they offer a date, as the introduction of the term "thyroid" in 1646, where the introducer ought to be Wharton, not Warton. This historical approach gives a human interest to what would otherwise be a dry record of grammatical usage. Sometimes the authors go beyond their scope: particularly successful in this way are the miniature essays on the history of certain terms, for

instance, *muscle*—which traces the development of muscle-names from Galen who used few names for muscles, " . . . considering [them] in topographical groups and numbering the individual muscles of each group ", through Vesalius to Sylvius and Riolan, who " made attempts towards the introduction of a definite nomenclature " to Cowper, Douglas and Albinus who perfected it. But some of these notes give irrelevant information, for instance that on *mitral*, which describes the various ancient garments named *mitra*, only to conclude that : " The bishop's mitre, as we know it, . . . is the only one of the various forms of *mitra* to which the atrio-ventricular valve bears a resemblance ", or that on *stapes*, which discusses the Romans' ignorance of stirrups.

The list is remarkably comprehensive, although common english words and self-explanatory terms have been deliberately omitted. A few general scientific terms, such as " eugenics " and " phylogeny " have been put in, and so have some pathological eponyms such as " Parkinson's disease ", a random choice from a vast field. One lack might be made good in a new edition, hints for pronunciation. Greek long e and long o are sometimes marked, but many ambiguities remain. Disregard for uniformity is of less importance and may even bring home the variant meaning of a word in various contexts ; for instance, words ending in -oid are usually given as from the Greek for " shape " but under *pithecoid* this suffix is translated " like ". Similarly the list of references, recommending a well-chosen group of authorities, is set out regardless of uniform bibliographic style. There are a few minor mistakes and misprints, for example under *platycnemia*, where, as the context requires, greek " kneme " is in fact " shin " and not " knee ". No errors or omissions of importance have been detected, and the book can be warmly recommended as useful at first reading and of growing interest the more it is studied.

W. R. LeFanu

BLOOD-DONORS

1149 Der Blutspender

H. Willenegger & R. Boitel. Basel, Benno Schwabe & Co., 1947. 197 pages ; 48 illustrations. 22 x 16 cm. Sw. fr. 10.

(i) Historischer Rückblick; (ii) die Entwicklung des Spender- und Transfusionswesens nach Entdeckung der Blutgruppen; (iii) der Spender; (iv) die Organisation des Spender- und Transfusionswesens; (v) der Spende- und Transfusionsdienst in den einzelnen Ländern; (vi) der Spende- und Transfusionsdienst in der Schweiz; (vii) Schlusswort. Anhang.

The development of blood-transfusion services in Britain and the USA was greatly hastened by the demands of war. In Switzerland, amongst other countries, this special stimulus was lacking, and the transfusion service now finds itself comparatively backward. This situation has prompted the authors to review the whole question of blood-donation.

Before the war, donors were mainly of two kinds, namely, relations or friends of the patient, many of whom gave blood on one special occasion only, and professional donors, who gave blood regularly in accordance with a special tariff ; this varied greatly so that the price in 1937 varied—for example, from £7 per 500 cm.³ in New York to £1½ for the same amount in Berlin. In Portugal, it was worth as much as twenty days' paid holiday if the donor had never given blood before. In addition to these two types of donor, there were in Britain, Holland and a few other countries, donors organized by the Red Cross, who gave their blood free of charge. Under war-conditions it was necessary to recruit very large numbers of donors to supply blood for production and storage of plasma. As a result, blood-donation became highly impersonal, and education of the public was needed to bring home to them the way in which medical services had come to rely on having stored blood and plasma constantly available. Now, in peace, the public must be made to feel that blood-donation by healthy adults has become a social duty. The appeal that was made so successfully in time of war must succeed in peacetime, and it is essential to learn how to appeal to the same philanthropic motives in potential donors.

There is a very interesting history of blood-transfusion, containing some details which do not appear in many accounts ; for example, there are particulars of the first transfusion from one human to another, which was carried out in 1823 by James Blundel, Professor of Physiology and Obstetrics at Guy's Hospital, London.

The book is obviously meant for the lay reader as well as for doctors, and it therefore contains only a short description of the blood-groups. Nevertheless, one feels that the Rh factor is altogether too summarily dismissed for a book published in 1947. Moreover, the statement that one occasionally meets a naturally-occurring anti-Rh antibody of the cold-agglutinin type is untrue no certain case of a naturally-occurring anti-Rh antibody having yet been described. Nevertheless, criticism of small details must not be allowed to obscure the impression that this is a well-informed book which gives one of the best available accounts of the development of blood-transfusion.

Finally, it is impossible to avoid mentioning the striking cover. This shows one shadowy figure pouring out red lines of blood from his heart to a stricken man below. This conveys excellently the feeling of the life-saving importance of blood-transfusion.

P. Mollison

CANCER : AN UNCONVENTIONAL VIEW

1150 Metabolic Therapy of Cancer

Ernst Freund. London, Daniel Godwin, Ltd., 1946. 178 pages. 22 x 14 cm. 12s. 6d. [£0.625]

(i) Cancer cells and blood serum; (ii) chemistry of the active factors in the cytolytic reaction; (iii) correlation between carcinolytic and carcino-protective factors; (iv) carbohydrates and carcinoma; (v) origin of lytic and protective components of sera; (vi) specific intestinal flora and malignant tumours; (vii) chemistry of predisposition for cancer; (viii) influence of intestinal acids on growth; (ix) metabolic interpretation of tumour growth and interpretation of clinical phenomena; (x) the Freund-Kaminer diagnostic reaction; (xi) metabolic cancer therapy.

The name of Ernst Freund recalls a phase of cancer research which has, for a time, occupied a position of influence. To modern generations of cancer research-workers, Freund's theory of tumour-etiology, the Freund-Kaminer sero-diagnostic test, and the suggested principles of therapy based on these investigations, are perhaps less well-known. An english translation of a book by the originator of this half-forgotten chapter of cancer research, might, therefore, appear both timely and desirable.

As mentioned in the preface of the book, the investigations arose from an early observation by the author in 1885, while he was still a student. It ended half a century later with the ambitious exposition of the cause, diagnosis, and treatment of cancer. Underlying these researches was the idea that normal serum caused lysis of cancer cells, while serum from cancer patients not only failed to produce this effect, but actually protected such cells from the lytic action of normal serum. This eventually formed the basis of the Freund-Kaminer sero-diagnostic test for cancer. Freund believed, moreover, that " instead of confining ourselves to an investigation of the action of the malignant cell on the organism, we ought to investigate the action of the organism on the malignant cell ". This directed his attention to the anabolic processes of the living cell, and led him to the study of dietetic and other extraneous factors from which the cell builds up its characteristic protoplasm. An analysis of the " carcinolytic " factor in normal serum, and of the " anticarcinolytic " or " protective " factor in cancer serum, led Freund to the conclusion that the former was a saturated, and the latter an unsaturated dicarboxylic acid, each bound to some other component (euglobulin or nucleoglobulin) in the serum. These dicarboxylic acids he considered to be formed in the intestine by bacterial action, and an examination of the bacterial flora of cancerous and normal people pointed to the presence of a specific type of *B. coli* in the former, which he held to be responsible for the formation of the unsaturated acid—thus representing a predisposition towards cancer. This, in turn, led him to formulate a special dietetic regime for cancerous patients.

It is not the purpose of this review to analyze the complicated evidence on which these views are based, nor to offer an appraisal of the theories resulting from this work. That could be left to a detailed assessment of the voluminous literature which has already accumulated on the subject. The reader will, however, be disappointed if he expects such an unbiassed survey in the present book.

It may be asked, then, for whom this book was intended. Not for the lay public, nor for the medical student, since it represents a highly specialized and one-sided approach to the cancer problem. Nor as a guide to the clinician or clinical pathologist, since the practical value of the Freund-Kaminer sero-diagnostic test has greatly diminished with the passing of time, while the therapeutic applications have never commanded serious attention, and are in definite conflict with modern researches on the subject. The medical historian, who may seek a balanced perspective of this complicated field, or the experimental scientist, who may desire to learn more of this work in the hope of being able to salvage any truths that may lie hidden in this vast store of experimental data, will both be disappointed in this book, and will turn rather to the existing books and reviews (e.g. by Stern & Willheim, Hirszfeld, and others), in which the literature on the subject is more fully presented, and in which some attempt, at least, is made to evaluate the conflicting claims of different authors.

The translation into English is admirably performed, but greater care might have been taken in the accuracy of the scientific terminology.

I. B.

CARDIOVASCULAR DISEASE

1151 Cardiovascular Disease in General Practice

Terence East. Second Edition. London, H. K. Lewis & Co. Ltd., 1946. x + 198 pages; 40 illustrations. 21 × 14 cm. 12s. 6d. [£0.625]

(i) The interpretation of symptoms; (ii) physical examination of the heart; (iii) heart failure; (iv) the treatment of heart failure; (v) failure of the coronary circulation; (vi) peripheral failure; (vii) the infections of the heart; (viii) subacute bacterial endocarditis; (ix) syphilis; (x) chronic valvular disease; (xi) pericarditis; (xii) hypertension; (xiii) thyrotoxicosis; (xiv) auricular fibrillation and flutter; (xv) ectopic disorders of rhythm; (xvi) disorders of conduction; (xvii) the cardiovascular system in anaemia, chronic pulmonary disease, chronic renal disease, minor infections, anaesthesia, pregnancy, athletics, deficiency conditions; (xviii) diseases of arteries and veins; (xix) congenital diseases of the heart; (xx) the heart in middle age and onwards; (xxi) some aberrations and the normal heart. Index.

The specialist called to write for the general practitioner is in a dilemma. Dealing with a subject like cardiovascular disease, he should write about it as a general practitioner is likely to see it. In Britain, this means that electrocardiographic detail should be omitted, and common conditions should be discussed fully. At the same time a tendency to "write down" the subject for the general practitioner should surely be avoided. The general practitioner has had the same basic education as the specialist, and is often capable of understanding more about the rationale of diagnosis and treatment based on pathological and physiological principles than he is given credit for. The practitioner who takes the trouble to read monographs prepared for him should be given enough detail to stimulate his interest in his own particular approach to the problem.

Dr. East writes clearly and vividly in this little book. He points out that the head of the poet Alfred de Musset shook with his Corrigan pulse, but unfortunately he does not instruct the doctor on how to look for and interpret capillary pulsation. Lengthy accounts are given of coronary thrombosis and subacute bacterial endocarditis, but there is no mention of penicillin therapy.

The chapter on hypertension should have been considerably larger than that given, in view of the fact that this condition is now the "Captain of the men of Death". One instrument which the practitioner should have and use is surely an ophthalmoscope, and yet only six rather poor lines are given to the examination of the retina which is so valuable in diagnosis and prognosis. Thrombophlebitis is a common and troublesome condition for the general practitioner, and one which he should understand as fully as possible, and yet the condition is here disposed of in about half a page. Our tendency to take little interest in this condition may be due to the fact that heparin and other anticoagulant measures in treatment have been impossible to apply in Britain for economic and other reasons.

It is easy to be critical. Dr. East writes well and his opinions are sound. The general practitioner who reads this book will be the better for it, but he will have to seek a good deal more information elsewhere if he is to understand the diagnosis and treatment of cardiac patients in general practice.

1152 Heart Arrhythmias in Children

Acta Paediatrica, 1947, **34**, Suppl. 1

Bernhard Landtman. Helsingfors, Mercators Tryckeri, 1947. 107 pages; 17 figures. 23 x 14 cm.

(i) Material and method; (ii) sinus arrhythmia; (iii) extrasystoles; (iv) flutter and fibrillation; (v) paroxysmal tachycardia; (vi) conduction disturbances; (vii) rare arrhythmias; (viii) heart action in premature infants. Summary. Literature.

Within the period 1936-1946, 5,600 children under the age of 16 years were examined at the Heart Station of the Crown Princess Lovisa's Children's Hospital, Stockholm. Impressed by the disparity between the state of knowledge of the heart arrhythmias in adults and children respectively, Dr. Landtman set himself the task of analyzing the data obtained from the examination of these children with special reference to the frequency of occurrence of the different types of arrhythmias and their clinical manifestations. The present monograph is essentially a presentation and an appreciation of the findings in the 126 children (2.25 % of the total) in whom pathological arrhythmias were observed.

The account of each arrhythmia is prefaced by a succinct preamble which includes comments on the physiological or pathological processes involved and a fairly complete survey of the relevant literature. The date of the present investigations are then presented and a discussion and evaluation added.

Sinus-arrhythmia is considered in relation to age and the state of the heart, whether normal or diseased. The conclusion supported by statistical examination of the findings indicates that sinus-arrhythmia is more common in later than in earlier childhood, thereby confirming a similar observation published by Mackenzie in 1902. The data suggest that sinus-arrhythmia is less common in children with congenital heart-disease and rheumatic heart-disease than in normals although, as the author appears to realize, the numbers of observations are too small upon which to base a firm statistically-significant conclusion.

Extrasystoles were found in 1.5 % of the cases, the ventricular type being more common than the supra-ventricular (including nodal) type. The author conforms with common usage which allows the rather loose application of the term "extrasystole" to a beat arising from an ectopic focus and to a premature beat, as well as to an interpolated premature beat or true extrasystole. This is unfortunate, since a further breakdown of the data might have helped to throw light on the difference in prognostic significance, if any, between the different types of premature beats or extrasystoles.

Nine cases of complete auriculo-ventricular block in children, whose ages ranged from a few hours to 11 years, are added to the literature. The author, with good reason, believes them to be examples of congenital block. However, the basis for the conclusion that the usual cause of the block in these cases is a septal defect may be questioned on the ground that the diagnosis of a septal defect seems to have been made largely, or entirely, from phonocardiographic investigations of a systolic murmur which was present in all the cases. Admitting the assistance which phonocardiography may lend to clinical diagnosis, and the technical advances made by Mannheimer and his group, whose methods were followed in this work, the clinician will require more convincing evidence of the existence of a septal defect than phonocardiographic demonstration of a systolic murmur.

An interesting and valuable chapter is devoted to heart-action in premature infants. From his observations on 63 premature infants, of whom 53 were less than one month old, the author concludes that disturbances in heart-action are not more usual in premature than in full-term children.

Two new cases of the interesting and uncommon condition of interference-dissociation in boys aged 7 and 15 years respectively are described in the chapter on rare arrhythmias. In one of these cases the arrhythmia disappeared spontaneously; in the other, vagal depression and sympathetic stimulation restored normal rhythm.

While this work discloses nothing which was not known before, it is a worthwhile contribution to the subject in the sense that it is a record of a relatively large number of carefully-analyzed observations from which no unwarranted conclusions have been drawn.

The translation into English, while at times erratic, is on the whole adequate.

1153 Heparin in the Treatment of Thrombosis: An Account of its Chemistry, Physiology and Application in Medicine

J. Erik Jorpes. Second Edition. London, Geoffrey Cumberlege, Oxford University Press, 1946. 260 pages; 24 illustrations. 22 x 14 cm. 18s. [£0.9]

Part I. The chemistry and physiology of heparin. (i) The discovery and chemistry of heparin; (ii) the mode of action of heparin; (iii) the site of formation of heparin; (iv) the strength of pure heparin and similar anticoagulants; (v) miscellaneous clinical uses of heparin; (vi) dicumarol, the haemorrhagic agent causing "sweet clover disease". Part II. Heparin and thrombosis. (vii) Heparin in the treatment of thrombosis; (viii) heparin in latent thrombosis, in pneumonia and other inflammatory conditions; (ix) the prevention and treatment of thrombosis with dicumarol; (x) some aspects of the pathogenesis of thrombosis and of its treatment; (xi) social aspects of thrombosis. Bibliography. Index.

The first edition of this book, published in 1939, was almost entirely devoted to the chemical and physiological properties of heparin—a field in which Dr. Jorpes is the acknowledged master. In the last few years, however, the treatment of venous thrombosis and pulmonary embolism with heparin, very largely the work of the pioneer studies of swedish workers, has undergone a profound change. Part II of the second (1946) edition of Dr. Jorpes' book, which occupies some two-thirds of the much-enlarged volume, deals with the place of heparin and dicoumarol in the prophylaxis and treatment of thrombosis. A most complete and fully-documented account of the development of the swedish work is given, and it is shown that both the immediate mortality and, more importantly, the late morbidity of deep venous thrombosis, which is apparently particularly common in Sweden, can be largely prevented. Dr. Jorpes draws attention to a fact which deserves to be stressed, namely that pulmonary embolism following deep venous thrombosis is met with as frequently on the medical side as on the surgical side of a general hospital. A feature which should be of particular interest to clinicians is the chapter on the social aspects of thrombosis, wherein it is shown that the average case remains in hospital 6 weeks, with an annual loss to the swedish nation of 600,000 dollars exclusive of lost working-time. There are about 5,000 new cases of thrombosis annually in Sweden, with a net loss of efficiency greater than that arising as the result of road-accidents of all kinds. A form of therapy by which the period in hospital is shortened to 5–10 days, and the frequency of such complications as induration and ulcer is strikingly reduced, assumes a position of social and even national importance. The data upon which conclusions are based are fully given.

The first part of the book deals with the chemistry, physiology, mode of action and site of formation of heparin, and with the methods available for its biological assay. Much of the work here is Dr. Jorpes' own, and the story is fascinatingly and clearly unfolded.

This monograph is an example of the value of such complications, not only to the scientific worker in the same field, but to the teacher and the more general reader. The first edition is already well known to, and esteemed by, Dr. Jorpes' fellow-workers; the second should bring him into contact with a much larger number of physicians and surgeons who cannot fail to be interested in the problem.

CLINICAL PATHOLOGY

1154 Recent Advances in Clinical Pathology

By various Authors. Produced under the auspices of The European Association of Clinical Pathologists. General Editor, S. C. Dyke. London, J. & A. Churchill, 1947. xii + 468 pages; 34 illustrations. 21 x 13 cm. £1 5s. [£1.25]

Section I: Bacteriology. (Editor: Robert Cruickshank.) (i) Laboratory diagnosis of enteric infections; (ii) laboratory diagnosis of typhus fever; (iii) laboratory diagnosis of sore throat; (iv) serological classification of streptococci; (v) laboratory diagnosis of primary atypical pneumonia; (vi) laboratory diagnosis of pertussis; (vii) bacteriological diagnosis of tuberculosis; (viii) laboratory diagnosis of brucella infections; (ix) laboratory diagnosis of anaerobic infections; (x) laboratory control of pathogenic staphylococci; (xi) laboratory control of chemotherapy; (xii) laboratory diagnosis of leptospiral infections; (xiii) laboratory tests in venereal disease. Section II: Biochemistry. (Editor: E. N. Allott.) (xiv) Liver function tests; (xv) estimation of the prothrombin time; (xvi) control of the blood chemistry in gastro-intestinal disease; (xvii) excretion tests in Addison's disease; (xviii) biochemical aids in the diagnosis of nutritional deficiencies; (xix) crystalline forms and solubilities of sulphonamide derivatives; (xx) photoelectric colorimeters; (xxi) micromethods of blood analysis. Section III: Haematology and cytology. (Editor: B. L. Della Vida.) (xxii) Haematological nomenclature; (xxiii) the myelogram and its clinical applications; (xxiv) the Rh factor; (xxv) the transfusion of blood and blood products; (xxvi) blood grouping; (xxvii) the sedimentation rate of the red cells; (xxviii) the diagnosis of pernicious anaemia and the assay of liver extracts; (xxix) infectious mononucleosis and the differential Paul-Bunnell test; (xxx) the analysis of the semen; (xxxi) carcinoma cells in sputum and pleural fluid. Section IV: Histology. (Editor: A. H. T. Robb-Smith.) (xxxii) Aspiration biopsy in general tumour diagnosis; (xxxiii) cell counts in serial biopsies of carcinomata; (xxxiv) the lymph node biopsy; (xxxv) the testicular biopsy; (xxxvi) the endometrial biopsy; (xxxvii) the skin biopsy; (xxxviii) the peripheral nerve biopsy; (xxxix) the wet film technique in neurosurgery; (xl) the clinical and postmortem pathology of encephalitis; (xli) routine diagnostic technique of the general morbid anatomist. Index.

This new volume takes a worthy place in the well-known series of Recent Advances in various branches of medicine and surgery which Messrs. J. & A. Churchill have now been publishing for many years. Clinical pathology may be defined as the study of disease in the living patient by laboratory methods, and during the past eight years in Britain there has been a remarkable extension of the laboratory facilities available to clinicians, and without doubt in the future many more diagnostic laboratories will be established. The production of this volume is therefore timely.

The book is divided into four sections under section-editors who have correlated the work on bacteriology, biochemistry, haematology and histology. The bacteriological section deals with the modern methods used in the diagnosis of most of the common infections; each chapter is designed to deal generally with a particular problem followed by details of the technical processes in common use and ending with a representative list of references which should prove useful as a guide to further reading. It would, of course, be extremely easy to compile a list of methods to which no reference is made. Each clinical pathologist who attempts to follow the literature of pathology and bacteriology prepares for himself a survey of laboratory methods and their significance which he finds particularly useful. In a book of this size there are bound to be omissions, but here there are surprisingly few, and all laboratory workers will find a large number of methods which they will be anxious to try for themselves and which will lead inevitably to greater efficiency in their laboratories. There is one notable omission which is perhaps regrettable—there is no chapter on the recent developments in the laboratory diagnosis of the common virus-diseases. The simple staining-methods, the serological technique, and the use of the common laboratory-animals in the diagnosis of the virus conditions met with in medical practice will have to take their place in routine laboratory work, and a book of this type would have been a useful vehicle for the dissemination of this knowledge.

The section on biochemistry opens with an excellent survey of liver-function tests which will be as valuable to the clinician as it will be to the pathologist. Another remarkable chapter summarizes our knowledge on the biochemical aids in the diagnosis of nutritional deficiencies. The list of references which conclude his cannot fail to prove extremely useful. Most pathologists will already be familiar, however, with Professor King's excellent book on microchemical methods, and the inclusion of some of these in the present volume might well have been omitted and the extra space used to amplify the chapter on blood-chemistry in renal and gastric conditions.

The section on haematology is perhaps the least satisfactory. Haematological nomenclature is still not uniform, but few pathologists will agree with the section-editor's description of the myeloblast, and drawings or photographs of the cells of the normoblastic and megaloblastic series would be useful in the next edition. The reader will wish that a chapter had been added on recent advances in the diagnosis of the haemolytic anaemias, on which a great deal of work has been done in the last ten years.

The section on histology is a mine of information for the pathologist. Among other chapters Dr. Robb-Smith contributes an excellent survey of work done on lymph-node biopsy. Professor Russell deals with her wet-film methods used on neurosurgical specimens, and Dr. Greenfield has written on the pathology of encephalitis.

Taken as a whole, this book is a notable contribution to the books on pathology published in Britain and there is no doubt that pathologists owe a debt to Dr. Dyke and to the European Association of Clinical Pathologists under whose auspices it has been published.

H. B. M.

1155 Chemical Methods in Clinical Medicine: Their Application and Interpretation with Techniques of Simple Means

G. A. Harrison. Third Edition. London, J. & A. Churchill Ltd., 1947. x + 630 pages ; 125 illustrations. 24 x 15 cm. £2

(i) Special instruments. Notes on apparatus, colorimeters, comparator, meoscope, microscope, pipettes, spectroscopes, etc.; (ii) routine chemical examination of urine: qualitative; (iii) proteins in urine: "albuminuria"; (iv) urinary deposits: calculi and concretions; (v) tests of renal efficiency; (vi) reducing substances in urine: glycosuria, lactosuria, pentosuria, etc.; (vii) interpretation of blood-sugar and blood-sugar curves; (viii) chemical tests in diabetes mellitus and control of insulin treatment; (ix) ketosis, acidosis and alkalosis; (x) blood and derivatives in urine; (xi) urines abnormal in colour. Drugs in urine; (xii) bile and urobilin in urine: efficiency tests of liver and bile passages; (xiii) tests of pancreatic efficiency; (xiv) indicanuria. Miscellaneous urine tests; (xv) chlorides. Inorganic constituents of urine; (xvi) collection, preservation and quantitative analysis of urine: (xvii) collection and preservation of blood; (xviii) blood: qualitative examination; (xix) blood analysis; (xx) treatment and chemical analyses; (xxi) chemical examination of cerebrospinal fluid; (xxii) milk analysis; (xxiii) gastric analysis; (xxiv) chemical examination of duodenal contents; (xxv) chemical examination of faeces; (xxvi) basal metabolism and metabolism experiments; (xxvii) pigmentations; (xxviii) miscellanea and conundrums. Appendix. Index.

A new edition of this well-known and valued handbook is a welcome event. The first edition appeared in 1930, the second in 1937, and since that time many new techniques have been introduced into chemical pathological practice, and new substances such as the sulphonamides have become so widely used that tests for them or their derivatives are continually called for. The present edition includes some ninety pages of new matter, and the colour-plates have been increased from three to five, but the author has by careful condensation avoided an unwieldy increase in the size of the volume.

Revision has been thorough. New sections appear upon sulphonamide crystals in urinary deposits, methaematuria and myohaemoglobinuria, methaemalbuminuria and familial methaemoglobinaemia, the copper sulphate specific-gravity method for determination of serum-proteins, and the metabolism of chlorides, calcium, phosphorus and iron, to mention but a few topics. It would seem that nothing of real importance has been omitted.

Rearrangement and revision is noticeable in many sections, and the subject of pigmentations has been assigned a chapter to itself with two excellent colour-plates. The reviewer knows from experience how widely scattered much of this information was, and welcomes the synthesis effected here. He would have liked to see, however, just one paragraph setting forth the principles and factors governing the hue of *normal* skin from different locations. These are rarely appreciated.

'Harrison' is a book written by a craftsman for his fellow-craftsmen and, as the author states in the preface, it is also his own journal in which many thoughts and observations have been set down. Born of a ripe experience and a faculty for careful observation these are both illuminating and helpful. Note for example (p. 96) the warning that chromium-plated syringes must not be used for this determination of blood-urea, since in contact with trichloroacetic acid they liberate gas !

In the face of so much indebtedness, criticism would seem ungenerous yet there are certain points which the reviewer needs must criticize. In the introductory Chapter 1, some ingenious home-made machines and several standard pieces of apparatus, including the Ogal colorimeter and Lovibond comparator are described. There is no mention at all, however, of any kind of photoelectric absorptiometer or colorimeter. This type of instrument is becoming more and more favoured and widely used, whatever its merits and demerits, and should have been described.

It is also felt that a better expression than 10/100 HCl could have been found for a ten-fold dilution of the concentrated acid.

It can hardly be expected that an examination for poisons should be included in a book of this size or kind—toxicology demands a textbook to itself—but the frequency with which barbiturates have to be looked for in urines or stomach-washings would surely justify the inclusion of directions for the necessary tests.

On p. 47 it is stated that Bence-Jones' protein contains all the amino-acids found in other typical proteins. The reviewer's experience supports statements in the literature that Bence-Jones' protein contains no methionine, or only traces at the most.

These are only minor points, and detract in no serious way from the great value of the handbook. It remains the standard work for the british biochemist in the clinical pathological laboratory, and this new edition will prove as indispensable as did the former.

Both author and publisher are to be congratulated upon the excellent paper, binding and type of the volume which they have produced for a sum not unreasonable for the present times.

1156 Die Milzpunktion: Technik, diagnostische und hämatologische Ergebnisse

Sven Moeschlin. Basel, Benno Schwabe & Co., 1947. 205 pages ; 119 illustrations. 21 x 14 cm. Sw. fr. 30

I. Allgemeiner Teil. (i) Historischer Überblick; (ii) Methodik; (iii) zellgenetische Probleme; (iv) Zellmorphologie des Milzpunktates; (v) Beobachtungen über Mitosen; (vi) das Splenogramm. II. Spezieller Teil. Das Milzpunktat bei splenomegalen Erkrankungen. (vii) Nicht entzündlich bedingte Milz-Hyperplasien; (viii) entzündlich bedingte Splenomegalien; (ix) Lymphogranuloma Hodgkin; (x) neoplastische Milzaffektionen; (xi) degenerative Erkrankungen der Milz; (xii) Speicherkrankheiten; (xiii) pathogenetisch noch ungeklärte Splenomegalien. Schlusswort. Zusammenfassung der Ergebnisse. Literatur-Verzeichnis. Sachverzeichnis.

This well-illustrated monograph on splenic puncture is written by an acknowledged authority in the field of haematology, who was one of Naegeli's assistants. It is attractively produced on good paper, and must fill british colleagues with envy. It is based on an experience of 180 splenic punctures, in 7 years, and on an extensive study of the literature on the subject. Moeschlin's rules for the use of this method are worth remembering :

i. Splenic puncture should be performed only if the spleen is definitely enlarged, and under fully sterile precautions.

ii. It should not be done in the presence of haemorrhagic diathesis, or of fresh, active infection or infarction, as indicated by pain in the splenic area.

iii. The patient must be fully conscious.

The history and exact procedure as well as problems of the development, origin and morphology of the cells met with in splenic-puncture material are discussed in the general section, and studies of mitotic figures and a series of normal and pathological splenograms are recorded. In the special section the changes which may occur in disease are described as they are reflected by splenic puncture. The non-inflammatory states include cirrhosis of the liver, haemolytic anaemia, pernicious anaemia, and the various forms of thrombocytopenia. Inflammatory splenomegalies include acute fevers with their neutrophilic reaction, infectious mononucleosis, epidemic hepatitis and other virus affections with their lymphatic reaction, and the more chronic inflammatory states, such as malaria and kala-azar. Tuberculosis, Boeck's carcoid, syphilis and undulant fever are grouped as the splenic granulomatoses. The chapter on Hodgkin's disease is followed by that on the neoplastic splenic affections, such as leukaemia, lymphatic and myeloid, polycythaemia vera, erythroblastosis and erythroleukaemia, and reticulo-endotheliosis, and includes notes on splenic sarcoma and other tumours. The special section closes with chapters on amyloid disease, Gaucher's disease, and other splenomegalies of as yet unknown pathology. Illustrative cases are reported with clinical notes, blood-pictures, and splenograms. Many are accompanied by myelograms and adenograms and other cytological and histological investigations.

Splenic puncture is of diagnostic value in certain cases, but keeping in mind the limits set by Moeschlin, a large number of cases of leukaemia, the disease par excellence in which splenic puncture can be of assistance in diagnosis and for the assessment of the progress, must not be subjected to it, because infarction of the spleen is such a common incident here. Among the 180 cases there are, therefore, only 9 with lymphatic and 13 with myeloid leukaemia.

If the diagnosis value of splenic puncture is thus narrowly circumscribed, it is still very interesting to examine splenic-puncture material and to study cellular morphology, and medical science will always benefit from such investigations, though much caution is needed.

The photomicrographs are of a very high standard and so are the coloured plates. The book will be of interest to clinician and pathologist alike, who will find in it much useful information.

E. Neumark

DENTAL SCIENCE AND TECHNOLOGY

1157 Special or Dental Anatomy and Physiology and Dental Histology, Human and Comparative Vol. II

T. W. Widdowson. 7th Edition. London, Staples Press Limited, 1946. xx + 333 pages ; 201 illustrations. 21 x 13 cm. £2 2s. [£2.1]

(i) Comparative dental anatomy (introduction); (ii) definitions of terms used; (iii) horny teeth; (iv) functions of teeth; (v) homologies and definitions of mammalian teeth; (vi) deciduous or milk teeth; (vii) attachments of teeth; (viii) the animal kingdom: fishes; (ix) amphibia or batrachia; (x) reptilia; (xi) aves—birds; (xii) mammalia: prototheria; (xiii) metatheria; (xiv) edentata; (xv) ungulata; (xvi) cetacea; (xvii) sirenia; (xviii) carnivora; (xix) rodentia; (xx) insectivora; (xxi) cheiroptera; (xxii) primates; (xxiii) the evolution of mammalian teeth; (xxiv) special characteristics of skulls, bones and muscles of jaws, etc. Index.

"Widdowson" has long been the textbook for most students of dental anatomy. It now enters on its seventh edition further expanded, but Volume II with its emphasis on comparative dental anatomy changed the least. This latter part of the subject is rarely enthused over by the student and by many is regarded as outmoded. Some examining bodies have seen fit to curtail markedly the time given to it. The present text is in part guilty of a thwarting of the student's interest because of an uninspired cataloguing of the dentitions (together with the inevitable formulae) of the vertebrates. The keynote of the book is throughout a painstaking assembly of data and snippets of the views of workers in this field but it lacks a true digestion and integration. This is the more disappointing since comparative anatomy can do so much to give perspective to our dental studies of the human masticatory apparatus. To those who have sat at the feet of that doyen of comparative anatomists, Frederick Wood-Jones, this book of Widdowson's must always appear a very pedestrian effort, painstaking but uninspired. Nevertheless, while the inevitable examination continues to demand a smattering of understanding of the subject, the dental student will be grateful that in Widdowson he can find the answers to his immediate problems.

1158 Dental Materia Medica, Pharmacology and Therapeutics

Walter J. Dilling & Samuel Hallam. Third Edition. London, Cassell and Company Ltd., 1946. xvi + 360 pages. 19 x 12 cm. 13s. 6d. [£0.675]

(i) Introductory; (ii) antiseptics and disinfectants; (iii) astringents; (iv) antacids; (v) oral hygiene; (vi) caustics; (vii) bleaching agents; (viii) obtundents; (ix) mummifying agents; (x) treatment of infected root canals; (xi) haemostatics; (xii) counter-irritants; (xiii) vaso-constrictors; (xiv) local anaesthetics; (xv) surface anaesthetics; (xvi) central anodynes and analgesics; (xvii) hypnotics; (xviii) basal hypnotics; (xix) motor nervous depressants; (xx) cardiac and circulatory stimulants; (xxi) vaso-dilators; (xxii) respiratory stimulants (analeptics); (xxiii) drugs acting on para-sympathetic nerve-endings; (xxiv) drugs influencing the digestive system; (xxv) emetics; (xxvi) purgatives; (xxvii) intestinal astringents; (xxviii) intestinal sedatives; (xxix) vitamins; (xxx) hormones influencing metabolism; (xxxi) treatment of anaemias; (xxxii) treatment of syphilis; (xxxiii) treatment of malaria; (xxxiv) vaccine and serum therapy, antitoxins; (xxxv) temporary filling materials and protectives; (xxxvi) Plaster of Paris; (xxxvii) oral secretion and excretions; (xxxviii) poisons, symptoms and treatment; (xxxix) Dangerous Drug Acts, poisons rules.

The third edition of this textbook does not differ markedly from earlier editions. From the dental surgeon's point of view, there is much that comes rarely within his normal field of experience. In those matters wherein he is more intimately concerned, a more detailed treatment would have been welcomed. The newer anaesthetics, tri-chlorethylene and cyclopropane are cases in point.

Specific criticisms[1] are : " oz." [ounce] and " ℥i " [ounce] are not synonymous (p. 15). In [british] pharmacy the rule is to employ the Imperial system when the term ounce is used and the Apothecaries' system when the sign ℥i is used. Therefore in the case of solids, 1 ounce = 437.5 grains and ℥i = 480 grains, a difference of nearly 10 %. One doubts if it is really advisable to use mercuric chloride as a mouthwash (p. 73). It is a dangerous poison, and safe substitutes, with greater antiseptic powers, are now available. Pages 80-83, the section on penicillin, does not accurately reflect our latest knowledge on the subject. For example, pure penicillin and even the impure forms are very stable if dry. As now supplied, there is no necessity to keep it in a refrigerator. Investigations show that there is no perceptible loss of potency even after many months' storage at ordinary temperature. Other preparations, if no water is present, are equally stable. The pastilles with a glyco-gelatin base are unstable and have been replaced by the lozenges, of which no mention is made. In dental practice the 50-unit lozenges are becoming very much in demand as a prophylactic measure before and after extraction. One rightly expects to find comments on their use and a possible criticism of their low strength. They are official in the British Pharmacopoeia.

Numerous other criticisms arise which cause one to feel that the dental facet of this volume is uncritical and in part ill-informed.

[1] [But the european reader may think that criticism might also, and possibly more usefully, be directed at the retention of these systems of mensuration.—Ed.]

1159 The Chemistry and Metallurgy of Dental Materials

J. Campbell Smith. Oxford, Blackwell Scientific Publications Ltd., 1946. vi + 317 pages; 60 figures. 22 x 15 cm. £1 1s. [£1.05]

Part I: Metals and Alloys. (i) Properties of metals, crystalline structure, space lattice; (ii) mechanical properties, tensile strength, elasticity, ductility, malleability, hardness; (iii) deformation of metals, slip bands, fatigue, hot and cold working, annealing, hardening; (iv) cast metal, ingots, crucibles, furnaces, pyrometry; (v) metallography, polishing, etching, micro-examination; (vi) theory of alloys, cooling curves, constitutional diagram, eutectic alloy; (vii) theory of alloys continued, solid solution diagrams; (viii) metals used in dentistry. Gold. Amalgamation, cyaniding, quartation, cupellation, wet assay, recovery, fluxes. Properties of gold, gold foil, colouring, electroplating; (ix) dental casting, investing, melting, casting machines; (x) gold alloys, calculations. Alloys with silver, copper, platinum, palladium, nickel; (xi) cast, clasp, and wrought golds, swaging, dies, and counterdies; (xii) heat treatment of dental gold alloys; (xiii) theory and practice of soldering, fluxes, blowpipe; (xiv) platinum group metals, silver, photography, mercury; (xv) dental amalgams, silver tin diagram, amalgam alloys, ageing, amalgamation; (xvi) amalgams, continued. Dimensional changes, packing, finishing, micro-structure, copper amalgams; (xvii) properties and alloys of copper, lead, tin, bismuth, antimony. Fusible alloys; (xviii) chromium, aluminium, iron; (xix) steel, thermal treatment, hardening, tempering; (xx) electro-deposition. Corrosion; (xxi) anti-corrosive metals, stainless steel; (xxii) stainless steel attachments, soldering, welding; (xxiii) nickel, cobalt, manganese, zinc, cadmium, magnesium, alkali metals. Part II: Inorganic Materials other than Metals. (xxiv) Boron, silicon, refractory materials; (xxv) dental casting investments; (xxvi) dental cements, zinc oxychloride, zinc oxyphosphate, silicate. Compositions, setting, pulp irritation; (xxvii) dental porcelain, composition, condensation, firing; (xxviii) impression materials, plaster of paris, setting, accelerators and retarders, casts, models; (xxix) other impression materials, rigid, plastic, elastic, quick setting stone, impression paste, hydro-colloidal materials, trays; (xxx) abrasives, dentifrices. Part III: Organic Materials. (xxxi) Rubber, vulcanization, synthetic rubbers; (xxxii) dental plastics, classification, chemistry of polymerization, acrylic resins, preparation, properties, processing; (xxxiii) waxes; (xxxiv) anaesthetics, inhalation, basic, local, novocaine and its analogues, adrenalin; (xxxv) pH value, buffer solutions, hypo-, iso-, and hypertonic solutions; (xxxvi) antiseptics and disinfectants; (xxxvii) organic chemistry. Hydrocarbons, halogen derivatives; (xxxviii) alcohols, ethers, aldehydes, ketones; (xxxix) fatty acids, acyl chlorides; (xl) unsaturated hydrocarbons, nitrogen and sulphur compounds; (xli) carbohydrates, sugars, starch, cellulose; (xlii) aromatic compounds, benzene and its derivatives, phenols, acids. Essential oils. Index.

One of the recent developments in dental education is the introduction in many dental schools of a course in the science of dental materials. The content of such a course is variable, and therefore the text-books designed to cater for such a course will necessarily show considerable variation of treatment. Doubtless, the present book was intended to meet the needs primarily of students at the Edinburgh Dental Hospital. Inevitably, the fact that the author is not a dental surgeon exposes him to the danger of a lack of perspective in the handling of the subject. In the reviewer's opinion this lack of perspective exists. A section on pure organic chemistry of 60 or more pages seems out of place. It is impossible to treat a subject like this adequately in 60 pages and to proceed, as the author does, from a definition of organic chemistry to the structural formula of chloro-6-hydroxy-3-toluene. In these days one has a right to presuppose an elementary knowledge of both organic and inorganic chemistry. Furthermore, it is extremely questionable whether the dental student is really helped by knowing the structural formulae of a number of unrelated therapeutic substances. The section on dental cements, impression materials, casting alloys, etc., contains much useful information and indicates many recent developments of knowledge in these fields. Nevertheless, there is a scrappiness of treatment, a lack of cohesion about this book which compels the reviewer to withhold from it the hall-mark of a first-class textbook. Several errors of spelling and, more important, of fact, occur in the text.

E. Matthews

1160 The Dental Assistant's Handbook

G. I. West. London, William Heinemann (Medical Books), Ltd., 1946. 108 pages; 25 illustrations. 19 x 12 cm. 6s. [£0.3]

(i) Introductory; (ii) surgery duties and sterilisation; (iii) psychological approach to patients; (iv) dental hygiene; (v) conservative work; (vi) the anatomy of teeth; (vii) dental radiology; (viii) anaesthetics—local and general; (ix) dental instruments and their care; (x) common dental diseases and abnormalities; (xi) mechanical work; (xii) dental formulae. Appendix. Index.

This is an excellent little book, full of commonsense in relation to the everyday problems that beset the dental assistant, i.e. dental nurse. As Miss West truly says, "A good assistant is the mainstay of a dental practice". Miss West emphasises the sense of responsibility that any good assistant must bear, both in relation to the patient and to her principal. If criticism there be of this book, it is that in parts it is likely to be too technical for the beginner. There would seem, for instance, to be little need for the inclusion of a description of such pathological conditions as epulis and ranula. Naturally, the treatment is in many respects superficial, and the suggestion that pyorrhoea is caused by an amoeba is unwarranted.

One deplores the advice given on page 32, that the assistant should complete her mixing of amalgam by doing so in the hand for 1 minute. Not only does such handling affect the setting-expansion and strength of the resulting amalgam-filling, but the risk of toxic absorption of mercury is a real one. This latter risk is recognized on page 78, where Miss West comments on the factors leading to mercurial stomatitis.

If, as seems inevitable, there is to be a great increase in the numbers of dental assistants, with the possibility of the scope of their work increasing on the lines of the dental hygienists trained by the RAF, then this little book, further expanded in a subsequent edition, will be found to be indispensable.

E. Matthews

DERMATOLOGY

1161 Practical Handbook of the Pathology of the Skin

J. M. H. MacLeod & I. Muende. Third Edition. London, H. K. Lewis & Co. Ltd., 1946. xix + 415 pages; 152 illustrations. 24 x 16 cm. £2 10s. [£2.5]

(i) Biopsies; (ii) methods for the histological examination of skin material in the fresh state; (iii) methods of preserving skin material for histological examination; (iv) methods of imbedding skin material and of cutting and preparing sections for staining; (v) general principles of staining skin; (vi) the cell and its mode of reproduction, and the method of staining the cell in general; (vii) the superficial architecture of the skin, the embryology of the skin as a whole, and a note on the development of the epidermis; (viii) the epidermis; (ix) the epidermis (continued); (x) pathological changes involving the epidermis: (xi) pathological changes involving the epidermis (continued); (xii) pathological changes involving the epidermis (continued); (xiii) pathological changes involving the epidermis (continued); (xiv) congenital anomalies of the epidermis; (xv) the minute structure of the corium; (xvi) the pathology of the corium; (xvii) degenerations of the cells and fibres of the corium; (xviii) pathological conditions of the corium; (xix) pathological conditions of the corium (continued); (xx) pathological conditions of the corium (continued); (xxi) hair; (xxii) pathological affections of the hair and the hair-follicle; (xxiii) the sebaceous glands; (xxiv) the sweat-glands or coil-glands; (xxv) the muscles of the skin; (xxvi) the blood-vessels of the skin; (xxvii) the blood in skin diseases and skin eruptions associated with affections of the blood-forming tissue; (xxviii) the lymphatics of the skin; (xxix) the nerve-terminations in the skin; (xxx) lipides or fat in the skin and subcutaneous tissue; (xxxi) the pigment of the skin; (xxxii) the nail; (xxxiii) parasitic diseases of the skin; (xxxiv) bacteria and the bacteriology of infectives kin diseases; (xxxv) streptotricheae, blastomycetes, and protozoa; (xxxvi) dermatophytes; (xxxvii) animal parasites of the skin. Index.

There are only a few slight changes in this edition. The second edition was published in 1940 and was exhausted four years later. It is not surprising that this book has been in great demand both by dermatologists and general pathologists. Text-books on general pathology and on morbid histology usually ignore the skin except for its tumours, and pathologists have long needed the help of such a book in reporting on the occasional specimens of skin sent to them.

Descriptions of histological technique are given fully and include methods of fixing and hardening specimens and a large range of staining-techniques. The histological changes found in the various dermatoses are dealt with more briefly. They will be of great help to a dermatologist in his early years, but are not intended to be used in the elucidation of difficult problems met in attempting to differentiate between rarities.

The book starts with an account of the performance of a biopsy and the details of the technique of preparing and staining a section from it. This is followed by a description of the epidermis and of its pathological changes. The corium and its disorders are then described. Next the appendages, vessels, nerve-endings, blood, fat, and pigment are dealt with similarly. The closing chapters contain an account of the vegetable and animal parasites of the skin. The excellent section on dermatophytes contains a useful table of the "common ringworm fungi" and an account of the appearances and diagnostic characteristics of the fungi both on direct examination and on culture.

The illustrations, both coloured and black-and-white, are profuse, clear, well chosen, and splendidly reproduced. I suggest that one of neurofibroma should be included in the next edition.

Other minor improvements which could be made in subsequent editions are :—(i) mention should be made of the presence of mucin in granuloma annulare; (ii) the histology of poikiloderma should be described; (iii) some account should be given of stasis dermatosis to help in differentiating it from Schamberg's disease and from Majocchi's purpura annularis telangiectodes.

The print, format, and binding are excellent. The quality of the paper is a marked improvement on that of the second edition. The style is simple and unambiguous. This is a good book and can safely be recommended.

E. Lipman Cohen

1162 Diseases of the Skin

James H. Sequeira, John T. Ingram & Reginald T. Brain. Fifth Edition. London, J. & A. Churchill Ltd., 1947. xii + 782 pages; 443 illustrations. 23 x 15 cm. £3 3s. [£3.15]

Introduction. (i) The normal skin, histology and physiology; (ii) morphology of skin diseases. Group I. Congenital abnormalities of the skin. (iii) Congenital abnormalities of the skin. Group II. Dermatoses of internal origin. (iv) Cutaneous affections in general diseases including vitamin deficiencies; (v) circulatory disorders, vascular and lymphatic; (vi) reticulo-endothelioses of the skin. Group III. Constitutional disorders. (vii) Eczema, pompholyx; (viii) neurodermatoses; (ix) lichen planus; (x) alopecia, leucodermia, sclerodermia, dermatomyositis; (xi) the seborrhoeic dermatoses; (xii) pityriasis rosea, psoriasis, keratodermia blenorrhagica, para-psoriasis; (xiii) toxic eruptions, including the erythemata; (xiv) erythrodermia and generalised exfoliative dermatitis; (xv) eruptions due to drugs. Group IV. Dermatoses due to external irritants. (xvi) Dermatoses due to mechanical and physical agents; (xvii) dermatoses due to chemical irritants; (xviii) occupational dermatoses and their medico-legal significance. Group V. Infective dermatoses. (xix) Affections caused by animal parasites; (xx) affections caused by vegetable parasites; (xxi) acute bacterial infections of the skin; (xxii) chronic bacterial infections of the skin; (xxiii) chronic bacterial infections of the skin (continued); (xxiv) chronic infective diseases of the skin; (xxv) chronic infective disease of the skin (tropical); (xxvi) virus diseases of the skin; (xxvii) dermatitis herpetiformis, pemphigus. Group VI. Atrophic and hypertrophic dermatoses, tumours of the skin. (xxviii) Atrophic conditions of the skin including ainhum; (xxix) hyperplasia and tumours. Group VII. Diseases of the appendages of the skin. (xxx) Affections of the sebaceous glands, hair follicles and sweat glands; (xxxi) diseases of the nails. Appendix I. Principles of general treatment and formulae. Appendix II. Principles of local treatment and formulae. Appendix III. Principles of physiotherapy.

Dr. Sequeira has had the assistance of two of his former pupils in preparing the 5th edition of his excellent textbook. The brief introduction sets the tone of the whole work—dermatology is closely related to general medicine, and "the psychological field" is of great importance in the behaviour of the skin. The other especially noticeable characteristic of the book is the lack of stress laid on allergy; this is a welcome change from those works which imply that an understanding of allergy is the most important requisite for the practice of dermatology. After a chapter on the normal skin and a helpful account of the morphology of skin-diseases, including twenty-one wise aphorisms, the rest of the book is divided into seven "groups" on the various dermatoses. Throughout, the descriptions of diseases and their diagnoses are clear and the sections on treatment are full, practical and really useful. The black-and-white figures are excellent, but some of the coloured plates could be improved. References are lamentably scanty.

The difficult subject of eczema receives unusually clear treatment without mentioning allergy. As elsewhere in the book, terminological muddles are avoided. It is a pleasure to see Besnier's prurigo described as such; "atopic dermatitis" is not mentioned. The only confusing name which has been retained is "white spot disease".

The three chapters on Dermatoses due to External Irritants are noteworthy. They include long lists of occupations, plants and external applications with accounts of the dermatoses which may result from them. The separate chapter on the medico-legal significance of the occupational dermatoses is unusual and

helpful. Tropical dermatoses are dealt with more fully than usual and are well illustrated. Syphilis receives seventy pages including three on prophylaxis. Treatment is described fully both with and without penicillin, and includes intensive courses.

There are three appendices—on general treatment, local treatment, and physiotherapy. A large number of useful prescriptions is given. Emulsion-bases are described and discussed. The principles of radiotherapy are given clearly and sufficiently. There is an index of 9½ pages.

New editions are certain to be required, and in them certain minor changes should be made—the myth that acne rarely lasts beyond the twenty-fifth year should be allowed to die; "ephelis" and "lentigo" should not be regarded as synonymous; reference to the Pastille method of measuring *x*-ray dosage should be omitted. A satisfactory classification of skin diseases has never been devised, but the arrangement of parts of this book seems to be rather strained.

This book can be recommended confidently to students and practitioners. Dermatologists will enjoy reading it and will appreciate the practical sanity of its outlook. The print, paper, binding and appearance are excellent.

E. Lipman Cohen

1163 An Introduction to Dermatology

Norman Walker & G. H. Percival. Eleventh Edition by G. H. Percival. Edinburgh, E. & S. Livingstone, Ltd., 1947. xii + 349 pages; 233 illustrations. 22 x 14 cm. £1 15s. [£1.75]

(i) Anatomy, physiology, and pathology of the skin; (ii) classification, diagnosis, and prognosis; (iii) treatment; (iv) erythematous eruptions; (v) the urticarias and purpura; (vi) the herpetiform and bullous eruptions; (vii) eczema and dermatitis—I; (viii) eczema and dermatitis—II; (ix) avitaminosis; (x) psoriasis, pityriasis rosea, lichen planus, pityriasis rubra pilaris, generalised exfoliative dermatitis; (xi) superficial bacterial infections and vaccinia; (xii) diseases due to animal parasites; (xiii) diseases due to vegetable parasites—I; (xiv) diseases due to vegetable parasites—II; (xv) infective granulomata; (xvi) tropical skin diseases; (xvii) the reticuloses; (xviii) disorders of the skin appendages—I; (xix) disorders of the skin appendages—II; (xx) disorders of the skin appendages—III; (xxi) dystrophic cutaneous disorders; (xxii) anomalies of sensation; (xxiii) benign cutaneous tumours; (xxiv) malignant cutaneous tumours.

Professor Percival collaborated with the late Sir Norman Walker in writing the 10th edition of this book. He has completely rewritten this edition and it is virtually a new book. It is an individual work and differs markedly in outlook from most other modern books on the subject. The approach is strongly morphological—"To diagnose a skin disease it is first necessary to determine what is the characteristic primary lesion." The histology is given for most of the conditions described. The macroscopic and microscopic descriptions of the various diseases provide the best sections of the book. Reference is rarely made to the patient who is almost ignored—"The history of a case of skin disease as obtained from the patient is of little importance except when it is confined to simple facts." Psychogenic factors receive extremely slight attention. The sections on topical applications are very good. On the other hand there is little suggestion of a close relationship between dermatology and general medicine—"in the vast majority of skin diseases the cause is located in or on the skin itself".

Of the twenty-four chapters the first three are of a general nature and the rest deal with the diseases of the skin. The chapter on treatment refers exclusively to details of external treatment—"in the majority of cases the most important form of treatment is the direct application of remedies to the diseased area . . .". This section is extremely helpful. The exact method of use of the various applications is described in full and is well illustrated. Many useful prescriptions are given and stress is laid on the value of starch-poultice, exact details being given for its preparation and mode of application to different parts of the body. Eczema and Dermatitis receive two chapters in which the nomenclature differs from the usual british custom—"it has been decided to use the term Eczema to indicate all those cutaneous eruptions presenting the eczematous type of dermatitis in its various forms". "On the other hand the term Dermatitis is restricted to examples of simple inflammation of the skin which present no distinctive feature of form or course . . .". Seborrhoeic dermatitis is regarded as a variety of infective eczema called "eczematide"—this is in line with the writings of french dermatologists. Besnier's prurigo also is regarded as a variety of eczema.

Throughout the rest of the book the arrangement and classification are as good as have ever been found. All descriptions are concise, but those relating to symptomatology, histology and external treatment are very clear. The paragraphs on etiology are less helpful, though allergy is treated with reasonable proportion. The most surprising statement is that the Senear Usher syndrome is identical with Pemphigus Foliaceus. The prognosis is given of each disease, acne being regarded unduly optimistically. Rarities are rightly ignored in a book of this size, and the relative amount of space given to the various dermatoses is well balanced except in two instances—leprosy receives more space than syphilis, and purpura deserves fuller treatment. No references are given. There is a good index.

The outstanding feature of the book is the excellent illustrations. These are profuse, admirably chosen, and clear. The unusually large number in colour are most satisfactory. As is to be expected in a work by Professor Percival, there are many first-rate photomicrographs. The print, paper, and binding are good. The book is exceptionally easy to handle.

E. Lipman Cohen

DISEASE IN CHILDHOOD

1164 Child Health

Edited by *Alan Moncrieff & William A. R. Thomson.* London, Eyre and Spottiswoode (Publishers) Ltd., 1947. 254 pages. 21 x 14 cm. 14s. [£0.7]

(i) Introduction: child health and the general practitioner; (ii) the organization of child welfare centres; (iii) common problems at a child welfare centre; (iv) the toddlers' clinic; (v) day nurseries and nursery schools: medical aspects; (vi) the work of the school health services; (vii) residential schools for handicapped children; (viii) the campaign against juvenile rheumatism; (ix) the diagnosis and management of mental deficiency; (x) the child guidance clinic; (xi) care of the new-born baby; (xii) tuberculosis in childhood; (xiii) venereal disease services; (xiv) the deaf child; (xv) the blind child; (xvi) the care of the crippled child; (xvii) physical education and the health of the child; (xviii) the control of the common fevers of childhood; (xix) breast feeding; (xx) artificial feeding of healthy infants; (xxi) "mixed feeding"; (xxii) diet and the school child. Index.

This small book is important, in the information it gives, and also in the implications and issues of policy it raises. It is therefore welcome both in what it achieves, and for the wider objectives it opens out. Under the title Child Health, it is a detailed and practical outline of the work of the many organizations dealing with infant- and child-care, written in each case by the medical officers engaged in these activities. These agencies include not only the "preventive" clinics of the child-welfare and school-health services, but also the "curative" clinics dealing with tuberculous, rheumatic, crippled, mentally-defective, and other types of handicapped children. The articles first appeared in *The Practitioner*, and now after suitable adjustment, and supplemented by an additional group of four articles on food and diet in infancy and childhood, are gathered into the present volume under the editorship of Professor Moncrieff and Dr. Thomson under the comprehensive title of Child Health.

There have been many theoretical discussions of what Child Health is, or ought to be; and of its policy. Here in this book we have an account of what is being actually done by organized medical and nursing services to safeguard the health of children. The account is written by men and women engaged in the conduct of these services, and is permeated by a critical and moderate spirit. Such an authoritative account of what is being done today in the field of Child Health must be of value, showing what is good, and not hiding what is faulty. After reading these many papers, some general impressions may be given. One is of the satisfactory gradual extension of the supervision of infants to the years between one and five so that the whole life of childhood before and during school is now coming under a continuous survey in clinics. Another is of the established and growing popularity of the preschool clinics among mothers. A third impression is of the enormous mass of minor defects and disorders discovered and successfully dealt with by these clinics and of the great contribution made thereby to the better health of infants and children.

What of the future development of this work? So far as the diagnostic and remedial parts are concerned, it is evident that

an elaborate and successful machine has been built up; and in the future, nothing better is likely to replace it. But the work has also its educational side, moving towards the eradication of these innumerable blots and blemishes in child life; and here there is a general feeling, expressed in this book, in official reports, and in the new National Health Service Act, that the final goal of radical prevention will be more quickly reached by setting up within the home a service of education under the aegis of the home doctor (the family practitioner) and the health-visitor. For it is within the home—in its physical conditions, and in the personal aptitudes of the mother—that the laws of child health are seen in operation; and it is the degree of observance paid to these laws within the home that determines the issue of health or disease in the child. It is widely realized, therefore, that the new national medical service brings to the general practitioner an opportunity of making an important contribution to child health. These implications and ideals and their practical fulfilment are discussed in the opening chapter of the book by Sir Leonard Parsons. In a judicial and comprehensive survey, he discusses the present position of the child-health services, and the present and future position of the general practitioner with regard to them. But it should be made clear that in the future the general practitioner may participate in this field of preventive child-medicine in two ways, by taking a share in the existing child clinic-services, and by advising mothers and supervising children in their homes.

It will thus be seen that the book under review deals with a medical problem of national importance and is a valuable contribution to the problem. It gives an authoritative survey of the organized services in the field of child health. It also raises important issues of future policy which are of particular concern to the general practitioner.

Charles McNeil

1165 Diseases of Children

Edited by *Sir A. E. Garrod, Frederick E. Batten & Hugh Thursfield.* Fourth Edition edited by *Donald Paterson & Alan Moncrieff.* Vol. I. London, Edward Arnold & Co., 1947. xi + 771 pages; 154 illustrations. 23 x 14 cm. £1 10s. [£1.5]

Part I. General considerations. (i) Heredity; (ii) vital statistics and administrative aspects; (iii) growth and development; (iv) the use of drugs in infancy and childhood; (v) clinical pathology; (vi) water and electrolyte control and acid-base regulation; (vii) septicaemia, pyaemia and toxaemia; (viii) practical procedures; (ix) anaesthetics in the surgery of children; (x) the feeding of infants and children. Part II. Diseases of children. (xi) The newly-born baby; (xii) diseases of nutrition; (xiii) disorders of metabolism; (xiv) diseases of the ductless glands; (xv) disorders of the alimentary system; (xvi) congenital defects of the alimentary tract; (xvii) diseases of the alimentary tract; (xviii) diseases of the nose, pharynx, larynx and ears; (xix) diseases of the respiratory system; (xx) tuberculosis; (xxi) allergy. Index.

We welcome a new edition of this well-known british textbook after an interval of 13 years. Advances in paediatrics during this period have been so extensive that much revision has been necessary, and many sections have had to be entirely re-written. The resulting increase in the amount of subject-matter has necessitated division of the book into two volumes. Volume I, which is now published, deals in the first place with matters of general consideration. At the present time when the importance of child-health is being stressed and emphasized, the chapter on vital statistics and administrative aspects is most opportune. Dr. Charles reviews in an able and lucid manner the statistical background leading up to present knowledge, he outlines briefly the origins and development of the Child Welfare Services, and points out some of the problems that have yet to be solved. The newborn baby and diseases of nutrition, and the alimentary and respiratory systems, are considered in the second part of this volume. There is a very useful chapter on practical procedures, including parenteral administration of fluid, lumbar and cisternal puncture, artificial respiration, etc. Throughout the book an even balance of the various subjects and diseases is maintained, and the re-duplication, inevitable and not always undesirable in any book of this character, has been kept within reasonable proportions. There is a good selection of photographs, diagrams and illustrations, and references to current literature are given at the end of each chapter.

As an exposition of current british teaching and practice this book can be confidently recommended, for both students and practitioners.

J. M. S.

1166 Diseases of Children's Eyes

James Hamilton Doggart. London, Henry Kimpton, 1947. xvi + 288 pages; 210 illustrations. 24 x 16 cm. £2 2s. [£2.1]

(i) General principles of examination; (ii) anatomy of the orbit; (iii) the eyeball; (iv) the eyelids. Conjunctiva. Lacrimal apparatus. Extrinsic ocular muscles, and Tenon's capsule; (v) the visual pathway and other nervous connections of the eye and its adnexa; (vi) development of the eye and its adnexa; (vii) developmental errors of the whole eyeball and of structures in close anatomical relation thereto; (viii) congenital abnormalities of individual structures of the eyeball accessible to external examination; (ix) congenital abnormality of intra-ocular structures not visible by external examination; (x) ocular complications and sequels of disease elsewhere; (xi) methods of treatment; (xii) ocular welfare; (xiii) injuries of the eyeball; (xiv) diseases of the orbit; (xv) refraction; (xvi) disordered movement; (xvii) incomitant squint; (xviii) concomitant squint; (xix) heterophoria and convergence defect; (xx) nystagmus; (xxi) lacrimal disorders; (xxii) disorders of eyelids; (xxiii) diseases of the conjunctiva; (xxiv) phlyctenular disease; (xxv) diseases of the cornea and sclera; (xxvi) the anterior chamber: juvenile glaucoma; (xxvii) diseases of the lens; (xxviii) diseases of the vitreous; (xxix) diseases of the uveal tract; (xxx) hereditary and familial disorders of the retina; (xxxi) other retinal disorders; (xxxii) diseases of the optic nerve. Index.

Ophthalmology of childhood has features which sharply distinguish it from ophthalmology in general. Childhood is greatly troubled with many congenital and genetic anomalies. The refraction of the eye changes markedly during the early years of life. Affections such as ophthalmia neonatorum, squint, phlyctenular ophthalmia, interstitial keratitis, spring catarrh and retinoblastoma fall particularly heavily or exclusively on childhood, and each of these affections illustrates a variety of pathological states to which the child is specially prone. In contrast, the abiotrophies are of little significance in childhood, and this also applies to iritis, cataract, and glaucoma, the major plagues of the adult and ageing individual. Physiologically and clinically, the eye and its adnexa show both considerable post-natal development and extensive senile degenerative changes, so that the field for a survey of eye-affections as seen in childhood is therefore fairly well defined, especially as the post-natal developments dictate a variety of pictures that differ from each other in the different periods of childhood.

So far no study of ophthalmology in childhood has appeared and Mr. Doggart is to be complimented on venturing on a task that must have appealed to many, who have felt baulked by the difficulties. The opening chapters of this treatise cover briefly but adequately anatomical, physiological and embryological considerations. The remaining chapters include, apart from the usual textbook classification, chapters on ocular complications of general disease and on methods of treatment. The chapters dealing with ocular muscle-imbalance are particularly good and full. The teaching is orthodox and well presented.

1167 Skin Diseases in Children

George M. MacKee & Anthony C. Cipollaro. Second Edition revised and enlarged. London, Hamish Hamilton Medical Books [1946]. xviii + 448 pages; 226 illustrations. 24 x 16 cm. £1 17s. 6d. [£1.875]

(i) The care of normal skin; (ii) diseases in which pyogenic bacteria are important etiologic factors; (iii) diseases due to fungi; (iv) diseases due to animal parasites; (v) allergic dermatoses in children; (vi) the eczema group; (vii) the erythema group of skin diseases; (viii) vascular diseases; (ix) dermatitis medicamentosa (drug eruption); (x) scaling dermatoses and the lichens; (xi) benign and malignant new growths; (xii) congenital cutaneous anomalies; (xiii) dystrophies; (xiv) pigmentary affections; (xv) diseases of the sweat glands, sebaceous glands, hair, and nails; (xvi) diseases of the mouth; (xvii) injuries due to physical agents; (xviii) vesicular and bullous diseases; (xix) contagious diseases; (xx) tuberculosis group of skin diseases; (xxi) syphilis in children. Index.

A second edition of this book (undated) has appeared with contributions from other american dermatologists. The preface states that the book is intended for the general practitioner and is therefore "essentially practical". This means in effect that little attempt is made at any general scientific approach to dermatological questions, and that the description of a disease is often a dreary list of unexplained symptoms. There are a number of points which might with advantage be clarified in any future editions. On page 78 it is stated that ". . . skin testing of patients with infantile eczema has been of much greater service in differential diagnosis than as a therapeutic aid." On the next page it is admitted that ". . . atopic individuals may be able to tolerate foods which elicit positive reactions, and it is also true that foods which fail to elicit reactions may nevertheless be responsible for

clinical symptoms." In this case, what aid to diagnosis has been afforded by the tests? Sulphathiazole ointment is recommended for impetigo and ecthyma on pages 20 and 23. The danger of sensitization is only briefly mentioned on page 71. Again, rosacea is grouped under the heading "Diseases involving pyogenic bacteria", and it is then said that "The most common cause of rosacea, perhaps, is the ingestion of stimulants . . ." Later it is added that there is often a vitamin-deficiency, a theory not borne out by the work of Fish.

In dealing with the treatment of diseases, this book shares with many other textbooks a depressing tendency to vague and woolly statements. For example, with regard to the treatment of furunculosis we read on page 25: "The various remedies that have been advocated as more or less specific (calcium sulfide by mouth, the arsenicals by ingestion or injection, mercury and calcium by injection, yeast, stannoxyl, turpentine, etc.) have been found of little value by those who have had sufficient experience, except, of course, when they are specifically indicated as a result of laboratory investigation." Now if the patient has syphilis, or anaemia, or calcium-deficiency, naturally he needs treatment, but apart from specific diseases what kind of laboratory investigation indicates the need for stannoxyl, turpentine, etc.? Chilblains are to be treated by ". . . attention to the general health . . ." Grey hair receives the same recommendation. As an "essentially practical" approach to the general practitioner I would like to suggest that we should all of us employ a recognized abbreviation for the following:—"The cause of this condition is largely (or entirely) unknown; in consequence, treatment is empiric and largely unsuccessful. Your guess is as good as another's." A famous President of the United States made some historic remarks about the difficulty of fooling all of the people all of the time. In deference to him, I suggest that we replace the above by "Verb. sap. Linc."

The book contains a useful inclusion on contagious diseases in childhood. There is an excellent chapter by Dr. Eugene Traub on congenital cutaneous anomalies. And the illustrations, with very few exceptions, are extremely good and helpful.

A. C.

ENDOCRINOLOGY

1168 Recent Advances in Endocrinology

A. T. Cameron. Sixth Edition. London, J. & A. Churchill Ltd., 1947. vii + 443 pages; 74 illustrations. 21 x 14 cm. £1 1s. [£1.05]

(i) Introduction; (ii) the thyroid gland; (iii) disease states associated with abnormal thyroid function; (iv) the parathyroid glands; (v) the islets of Langerhans and insulin; (vi) the steroid hormones and related compounds; (vii) the adrenal glands; (viii) the endocrinology of reproduction; (ix) the pituitary glands; (x) diseases correctly and incorrectly associated with hypofunction of the anterior pituitary; (xi) gigantism and acromegaly; (xii) Cushing's disease and the adrenocortical syndromes; (xiii) some other hormones and some related problems. Index.

Professor A. T. Cameron's books on biochemistry in its various phases have proved to be of the very greatest value to both medical students and their teachers. His *Textbook of biochemistry* is undoubtedly one of the best balanced works on the subject, and as an interpreter of the part played by biochemistry in biological and medical science he is perhaps without equal.

His contributions to the Recent Advances series has been equally notable and the present sixth edition of his *Recent advances in endocrinology* is precisely what we should expect from this author. The book covers the whole field of endocrinology, but it is obvious of course that the author is mainly interested in the chemical side. The rough plan which is followed throughout the book is that one chapter or section is devoted to each gland and the various hormones produced by it. The chapters are again sub-divided, the first sub-division dealing with the histological structure of the gland, the chemical nature of its secretions and its function in the normal human or animal body. The subsequent sub-divisions are devoted to the pathological states that arise through hyper- or hypofunction of the gland, the differentiation between the various symptom-complexes, and the appropriate methods of treatment.

In chapter 6 a general review of the steroid compounds is given, including not only the hormones of the adrenal cortex and the gonads but also the chemically-related sterols and vitamins D. A list of these compounds is given with their formulae, chemical names, the substances from which they have been isolated and the nature and extent of their biological activity.

The last chapter deals with the actual and presumptive hormones of the gastro-intestinal tract, the thymus and pineal glands, other suggested hormones and antihormones. The final section of this chapter emphasizes once again, as is done throughout the book, the close interrelationship existing between the various endocrine glands.

The documentation is excellent and is as up-to-date as possible. The volume can be used both as a textbook and as a work of reference. The complications of endocrinology are notorious, and of all subjects upon which it would be possible to write an incomprehensible textbook, endocrinology is certainly one. Professor Cameron has not only written a comprehensible work but a thoroughly readable volume. This is no mean achievement and one on which the author should certainly be congratulated.

E. C. Dodds

1169 Leitfaden für Zuckerkranke

Georg R. Constam. Basel, Benno Schwabe & Co., 1947. 127 pages; 15 figures. 22 x 16 cm. Sw. fr. 12.50

(i) Einleitung; (ii) das Wesen der Zuckerkrankheit; (iii) Ursachen der Zuckerkrankheit; (iv) Prophylaxe der Zuckerkrankheit; (v) die ersten Zeichen der Zuckerkrankheit; (vi) Verlauf der Zuckerkrankheit; (vii) Ziel und Prinzip der Behandlung; (viii) Technik der Harnuntersuchung; (ix) die Ernährung der Zuckerkranken; (x) Insulinbehandlung; (xi) andere "Heilmittel" gegen Zuckerkrankheit; (xii) Behandlung des Diabetes durch Operationen; (xiii) Koma diabeticum; (xiv) Komplikationen der Zuckerkrankheit; (xv) Zuckerkrankheit und Schwangerschaft; (xvi) Schlusswort; (xvii) Anhang. Sachregister.

The number of small books written for diabetic patients by doctors running diabetic clinics is legion in number and in form. The present swiss book under review seems to be the best ever produced in the german tongue in its thoroughness, clarity and humanity. The author is optimistic and hearty, and tells the diabetic reader that he can lead a normal life and can "hold his head high". He then proceeds in great detail to show the reader how this can be done, and includes all the usual sections of such a work—details of diet and admirable food-tables for a weighed and varied diet; the nature of diabetes, the action of different insulins, the use and care of the syringe, the necessary urine-tests; the complications of coma, foot-troubles and how to avoid them, and so on.

I wonder if the book, 126 large pages and produced with such good paper, print and illustrations as is impossible in post-war England, does not fall between two stools? Too much detail for the patient, and not quite enough to make it instructive to the doctor, nor enough to let the patient treat himself. Two pages on the differential diagnosis of coma seem out of place for the comatose patient or even his relatives. Hence the book goes in for greater detail, of doubtful value for the patient, than Lawrence's *Diabetic ABC* or the american books of Joslin or Wilder.

The diet-tables are all-inclusive and very well arranged. They give the weights of food-stuffs containing 10 grams of carbohydrate, protein and fat, and are thus arranged on the basis of the english system instead of the american percentage system. But a further column includes the percentages, very clear to the scientist but of doubtful value to the average patient. The source of the food-values is not mentioned, and the contents given vary considerably from the analyses of McCance & Widdowson used in Britain. It is difficult to make out the calorie-value of the diets advised (calories are hardly mentioned) or the different levels of carbohydrate and protein used.

As regards urine-tests, it is good to know that Benedict's test for sugar is ousting Nylander, Trommer and even Fehling's test, but it seems a pity that, for ketones, Rothera has not replaced Legal. It is impractical, too, to recommend the boiling of insulin-syringes instead of keeping them in 70% alcohol and so making a process of 20 minutes instead of 1. This is a minor criticism of the best book of its kind in the german language. There is nothing new in it for doctors, but it is practical, clear and helpful to the diabetic for whom it was written.

R. D. L.

FOODS

1170 Food and Health: An Introduction to the Science of Nutrition

A. Barbara Callow. Third Edition. Oxford, Clarendon Press, 1946. viii + 184 pages; 9 figures. 19 x 12 cm. 6s. [£0.3]

(i) Chemistry and nutritive value; (ii) digestion; (iii) food as fuel; (iv) vitamins and their history; (v) scientific standards for diets; (vi) the choice of food; (vii) everyday meals; (viii) diets for mothers and children; (ix) diets for special cases; (x) food habits and dietetic systems. Tables. Literature list. Index.

To write a book which is to be both intelligible to the lay reader and at the same time useful to the medical student, nurse, and dietician is a considerable task. Miss Callow has accomplished it in 146 pages (excluding tables, etc.) which are delightfully easy to read and which contain much sound practical advice. Beginning with a very simple account of the chemistry and nutritive values of the proximate dietary principles, the author takes us rapidly along the digestive tract to a consideration of food and the scientific principles upon which dietary standards are based. A chapter devoted to the vitamins contains a brief account of the development of the conception of accessory food-factors and their importance in modern diets, and this is followed by a superficial account of the special significance of vitamin A, aneurin, riboflavin, nicotinic acid, ascorbic acid and vitamin D. In this chapter it is surprising to read that ascorbic acid is not an acid, and that nicotinic acid is an alkaloid like quinine and cocaine. The following three chapters, The Choice of Food, Everyday Meals, and Diets for Mothers and Children are the best in the book, for they contain a good deal of wise and practical advice. The final chapter comprising a brief summary of diets suitable for convalescents and for the treatment of constipation, diarrhoea, obesity and gout is not so successful, probably because it is impossible to deal with these matters without going into more detail than would be suited to such a book.

A number of useful food-tables at the end of the book are compiled mainly from the *Chemical composition of foods* by McCance & Widdowson, and *Nutritive values of wartime food*[1] (His Majesty's Stationery Office). The figures refer mainly to british foods. A list of further more-advanced works to which the interested reader may turn for more-detailed information is appended. From this, however, is omitted *The vitamins in medicine*[2] by Bicknell & Prescott.

1171 Milk: Production and Control

W. C. Harvey & H. Hill. Second Edition. London, H. K. Lewis & Co. Ltd., 1946. viii + 512 pages; 211 illustrations. 25 x 16 cm. £1 17s. 6d. [£1.875]

(i) Composition of food value of milk; (ii) milk and disease; (iii) the cow; (iv) the cowshed; (v) the dairy; (vi) clean milk production; (vii) the distribution of milk; (viii) designated milks; (ix) the treatment of milk by heat; (x) laboratory and other control; (xi) legislation; (xii) future of the milk industry. Appendices. Index.

This issue is the second edition of a textbook which received a popular reception when first published in 1935. The authors, who are a Medical Officer of Health and a Sanitary Inspector, have collaborated very successfully in the production of this volume. As would be expected from such an association of authors, the aspects of hygiene and public health are kept well to the fore, and the book has supplied a much-needed want from the time of its first publication. It is evident that the authors have made a thorough study of the technical literature of their subject, and they have succeeded in presenting the textual matter in a sound and attractive manner so far as conditions in Britain are concerned.

Study of this volume should be particularly useful to advanced students of the production and handling of liquid milk, but many milk-producers, dairymen and dairy-technicians would gain a great deal by reading the book. In addition to chapters on composition and production of graded and ordinary milk, prominent features are chapters on the treatment of milk by heat, laboratory and other control, and legislation affecting milk. The book is well printed on good paper, possesses a good index, and the three appendices of 32 pages contain a wealth of practical information for public-health officials, advisory officers in dairying, and others employed in commercial dairying.

The authors are to be congratulated upon the production of a sound and accurate presentation of an intricate subject, and statements of too sweeping a nature are few in number. The chapter on legislation does not include industrial legislation associated with dairies, such as the Factories Act, Wages Council, Weights and Measures Acts, etc., but deals more with Acts and Orders connected with Food and Drugs, Public Health, and legislation during the recent war. Presentation of legal matters in a condensed form is notoriously difficult to achieve without distortion of the real meaning, but this work has been done well. Unfortunately, obsolescence usually develops very soon with such matter, and this case is no exception, and some of the wartime orders mentioned in the text have been included in the consolidation order, Milk (Control and Maximum Prices) (Great Britain) Order, 1945. S. R. & O. No. 410. Another instance where obsolescence could have been avoided occurs on page 190, and at least three of the list of advisory dairy-bacteriologists no longer hold the positions specified; in any future edition it would be better to delete the names of the advisory officers.

This volume is one which is worthy of a good reception and should be readily available for reference purposes in every public-health department. It is hoped that fresh editions will be issued from time to time and at intervals which are sufficiently short to avoid serious obsolescence.

F. Procter

[1] [For review, see *BMB* 773/154.—Ed.]
[2] [For review, see *BMB* 952.—Ed.]

INFECTIOUS DISEASES

1172 The Acute Infectious Fevers. An Introduction for Students and Practitioners

Alexander Joe. London, J. & A. Churchill Ltd., 1947. vii + 276 pages; 64 illustrations. 21 x 14 cm. 18s. [£0.9]

(i) Scarlet fever; (ii) erysipelas; (iii) puerperal sepsis; (iv) diphtheria; (v) whooping cough; (vi) cerebro-spinal fever; (vii) enteric fever; (viii) measles; (ix) chickenpox; (x) smallpox; (xi) vaccination; (xii) mumps; (xiii) rubella; (xiv) erythema infectiosum; (xv) serum reactions. Index.

This is a handy, readable little book with a good sprinkling of illustrations, likely to be popular with medical students making their first contact with the subject. The author's endeavour has been to answer the questions of the student and young resident medical officer, and he finds that, in spite of advances in the field of infectious diseases, these questions fundamentally remain constant.

This is, of course, perfectly true, but it is astonishing to what an extent the answers have been modified in the course of the last ten or fifteen years. This book is not too clear about the significance of these changes. With some notable exceptions they are all discussed, but too often without the conviction that comes from adoption or experience of them in practice. The profound effect of chemoprophylaxis and chemotherapy on acute otitis media, for example, cannot easily be realized when we are told that its incidence in scarlet fever and measles is 10%, a figure applicable to pre-sulphonamide days. In scarlatinal nephritis there is no mention of blood-urea, hypertension, salt-retention or encephalopathy. Too much space is devoted to erysipelas and its older forms which should now be defunct. Pulmonary collapse in pertussis is not even mentioned. The practice of radiography in fevers is hardly recognized. More serious is the apparent deviation of the author's practice from modern standards in the isolation-period of scarlet fever, and even of measles. Although the shorter isolation-periods are mentioned, it is not encouraging to be told that by the end of seven weeks only 70% to 80% of scarlet fever patients have returned home, and that many cases of measles are not fit to be discharged in less than three weeks.

These are examples of a certain conservatism pervading the book. Nevertheless, for its size, it contains a vast fund of information written up in an easy pleasant style. There are numerous references with name of author and date of publication scattered throughout the text, but no further details as to where they can be found. This seems to be another indication that the book is chiefly intended for the medical student.

1173 Infectious Diseases: with chapters on Venereal Diseases

A. B. Christie. London, Faber & Faber, Ltd., 1946. 324 pages; 4 illustrations. 22 x 14 cm. 12s. 6d. [£0.625]

Part I: Clinical. (i) Introduction; (ii) bacteriology: general; (iii) bacteriology: special; (iv) laboratory tests; (v) management of infectious diseases; (vi) streptococcal diseases; (vii) the control of streptococcal infections; (viii) staphylococcal diseases; (ix) diphtheria; (x) other throat complaints: glandular fever; (xi) measles—morbilli; (xii) rubella and mumps; (xiii) chicken-pox and smallpox; (xiv) diarrhoeal diseases: typhoid and paratyphoid fevers; (xv) diarrhoeal diseases: dysentery and food poisoning; (xvi) whooping cough; pertussis; (xvii) diseases of the central nervous system; (xviii) jaundice; (xix) influenza and pneumonia; (xx) undulant fever: typhus fever: anthrax; (xxi) common skin conditions; (xxii) nursery infections; (xxiii) tuberculosis; (xxiv) venereal diseases: gonorrhea and allied diseases; (xxv) venereal diseases: syphilis; (xxvi) special treatment of fevers; (xxvii) what to report; (xxviii) public health department. Part II: Social and Applied. (xxix) Carriers; (xxx) food and food-handlers; (xxxi) immunization; (xxxii) cross-infection; (xxxiii) infection in schools; (xxxiv) infection in the home; (xxxv) social aspects of infectious disease; (xxxvi) social aspects of tuberculosis; (xxxvii) social aspects of venereal disease. Index.

This book breaks new ground in the teaching of fevers to nurses. It deals not only with the clinical condition of the patient as seen in hospital, but also with the epidemiology and social aspects of the various diseases. It is clearly and concisely written. It is a book which a nurse can read quickly and enjoy.

The author gives sound advice as to the facts which must be committed to memory and those that can be deduced when once the underlying principles have been grasped. This is a praiseworthy aim, too often forgotten in the teaching of the nurse. The bacteriological data provide not only a general picture but are sufficiently detailed to act as a source of reference, which should help the nurse to co-operate intelligently with the doctor in each case as it arises. This is true also of many sections of the book. The clinical section includes not only the common fevers, but also tuberculosis and venereal diseases, the latter being treated in much more detail than is usual in nurses' textbooks. The section on the social aspects of infectious diseases, tuberculosis, and venereal disease is excellent. It gives information not hitherto available in books for the nurse training in fevers, and will certainly provide her with a wider view of the subject, which she will value particularly if she takes up home-nursing or health-visiting. It is pleasing to note that, on the subject of disinfection, the author has followed the recommendations of the Medical Research Council's War Memorandum No. 11. This may help to standardize teaching on this subject, which at present is confused. He recommends, however, two hours' rather than four hours' disinfection of excreta, a minor departure from the memorandum which hardly seems justified.

This book is highly recommended as a textbook for the fever-nurse and health-visitor. Its value will be enhanced if the author, in the next edition, can provide photographs of cases, or other illustrations.

1174 Human Torulosis. A clinical, pathological and microbiological study with a report of thirteen cases

Leonard B. Cox & Jean C. Tolhurst. Melbourne University Press. London, Geoffrey Cumberlege, Oxford University Press, 1946. xi + 149 pages; 67 illustrations. 25 x 19 cm. £1 5s. [£1.25]

(i) Introductory and historical; (ii) case reports; (iii) torulosis of various systems; (iv) microbiology of torula histolytica; (v) experimental torulosis; (vi) pathology of torulosis; (vii) laboratory diagnosis of torulosis; (viii) sources and routes of infection in torulosis; (ix) treatment of torulosis; (x) summary and conclusions. Appendix. Bibliography. Index.

Fungi were first recognized to be a cause of disease in animals and plants early in the nineteenth century, and subsequently there was much speculation as to the part they played in human diseases. Later in the century, as a result of the classical work of Pasteur, Koch, and Lister, fungi were eclipsed by bacteria as pathogenic agents in the field of medicine and at the same time mycology suffered a divorce from medical science to the detriment of both disciplines. It is only during the last two decades that modern mycological methods have been applied to the study of "medical" fungi, and shadows of the past are discernible on the useful monograph under review.

For example, the authors rightly state that a study of torulosis "should be of interest not only to the clinician, but to the pathologist and bacteriologist". It is also of considerable interest to the mycologist. Again, applied mycologists are showing increased appreciation of the stability and international uniformity which result from the use of specific epithets which conform to the international rules of nomenclature and it is unfortunate that the one selected by the authors for the torulosis organism is (as they suspect) never likely to prove internationally acceptable whatever the generic interpretations of the future. *Cryptococcus neoformans*, rather than *Torula histolytica* or *Cryptococcus hominis*, is the most appropriate name for the pathogen in question.

Torulosis is caused by a yeast-like organism. The skin, mucous membrane, lungs, or bone may be involved but typically there is infection of the central nervous system giving rise to a diffuse meningitis or meningo-encephalitis to which the sufferer usually succumbs. Local or widespread enlargement of the lymphatic glands, which in a significant number of cases is said to be Hodgkin's disease, frequently precedes, or is associated with, the disease and may hinder its recognition. Failure to recognize the disease is probably the reason why torulosis is considered to be so rare. It is widely distributed and there have so far been approximately one hundred published records covering the five continents. The greatest number of cases has been from North America, but the incidence is highest in Australia. Such conclusions should however be accepted with caution, as the statistics may well be representative of the interests of groups of workers rather than of the true frequency of occurrence of a disease which, like some other systemic mycoses, is liable to remain undiagnosed.

The present well-illustrated and well-documented monograph reports the histories of thirteen previously unpublished cases of torulosis encountered at the Alfred Hospital, Melbourne, since 1936, and summarizes the available clinical, pathological, and microbiological knowledge of the disease. It is a welcome addition to the literature of medical mycology and may well stimulate the monographic treatment of other mycoses.

G. C. Ainsworth

INTERNAL MEDICINE

1175 Further Studies in Encephalography

E. Graeme Robertson. Melbourne, Macmillan and Company Limited, 1946. x + 104 pages; illustrations. 24 x 18 cm. £2 2s. [£2.1]

(i) Ventricular filling determined by posture of the head; (ii) ventricular filling in flexion; (iii) ventricular filling with head erect; (iv) experiments in vitro; (v) factors producing the inflow of gas in vitro; (vi) an apparatus approaching more closely to the anatomical arrangement; (vii) demonstration in hydrocephalus; (viii) factors which may prevent ventricular filling; (ix) posture for filling the ventricles; (x) recent improvements in technique; (xi) the posterior fossa; (xii) the suprasellar region; (xiii) unusual path of entry to the ventricular system observed in hydrocephalus; (xiv) factors influencing filling of the lateral ventricles; (xv) pressure of the cerebrospinal fluid; (xvi) relationship of ventricles to the mid-line; (xvii) tumour or atrophy; (xviii) developmental abnormalities; (xix) anaesthesia for encephalography. References.

It was nearly thirty years ago that Dandy discovered the method of pneumo-encephalography. Since that time this technique received varying degrees of favour in different hospitals. All workers in the neurological field are agreed that this radiological investigation is of value, but there is a considerable discrepancy of opinion about the technique of introducing the gas, the type of gas to be used, and the type of patient suitable for the investigation.

Probably no one has used the method with such a wide application as Robertson. His new publication describes his experiences since 1941 when he published his first monograph on the subject—*Encephalography*. His material consists of 518 cases, 97 of which were shown to have intracranial space-occupying lesions, 28 of them infratentorial. There were no fatalities. The most revolutionary aspect of the work is the use of encephalography for the localization of infratentorial tumours. One cannot fail to be impressed by the author's courage in using this method. He states that he does it only with the co-operation of a neurosurgeon, and that many more cases must be examined before a final judgement can be passed. His further experiences will be awaited with great interest. Whatever the final outcome may be, Robertson has contributed much to our knowledge of the normal and abnormal appearances of the infratentorial cisternal spaces. His beautiful coloured illustrations are a work of art, and both the author and publisher are to be congratulated on the production of such excellent illustrations.

Many other aspects of encephalography are discussed, particularly the manner whereby the gas enters the ventricles and the

subarachnoid spaces. The observations are supported by experiments on the cadaver and *in vitro*. No one interested in neurology should fail to read this most stimulating and informative monograph.

James W. D. Bull

1176 Nutritional Disorders of the Nervous System

John D. Spillane. Edinburgh, E. & S. Livingstone Ltd., 1947. xv + 280 pages ; 103 illustrations. 25 x 16 cm. £1

(i) The vitamin B complex ; (ii) pellagra ; (iii) beriberi ; (iv) polyneuritis ; (v) Wernicke's encephalopathy ; (vi) nicotinic acid deficiency encephalopathy and allied states ; (vii) subacute combined degeneration of the spinal cord ; (viii) nutritional neuropathy in warm climates ; (ix) nutritional neuropathy in war-time ; (x) personal experience, 1942–46 ; (xi) personal experience (continued) ; (xii) the gastro-intestinal tract and nutritional neuropathy ; (xiii) general conclusions. Appendix—case notes. Author index. Subject index.

During the recent war large numbers of men and women were exposed to severe dietary restriction over long periods, and the effects of malnutrition could be observed on a scale far beyond the reach of experimental medicine and rarely encountered even in times of severest famine. Of all the deficiency diseases which resulted, the disorders of the nervous system are probably at the present time the most imperfectly understood.

None of the neurological syndromes is new ; reports from all parts of the world, appearing at intervals for more than a century, have indicated that defective nutrition may impair the function of the brain, spinal cord and special-sense organs, as well as the peripheral nerves. The author, in this monograph, brings together all the relevant information on this complex subject and, without ever being dogmatic, discusses the relationship of the nutritional neurological disorders to dietary deficiency, to known deficiency-diseases, to one-another and to certain other nervous diseases of obscure etiology.

The early chapters review, briefly but lucidly, the present state of knowledge with regard to vitamins in general, and vitamin-B complex factors in particular, to beriberi and pellagra, polyneuritis, Wernicke's syndrome and the encephalopathies associated with nicotinic-acid deficiency. The views expressed are, in the main, those generally accepted : the bibliography, well selected and full without being overwhelming, is worthy of particular attention, the author, in the course of his researches, having retrieved from obscurity a number of interesting and important, but little-known, papers. A chapter is devoted to subacute combined degeneration of the spinal cord ; the possibility of a nutritional basis for this condition is discussed, and its clinical similarity to certain nutritional ataxias is pointed out.

The author then turns to nutritional neuropathy in warm climates, and detailed descriptions are given of sensory ataxia, spastic paraplegia, the " burning-feet " syndrome, retrobulbar neuritis, and nerve deafness, as they have been observed in malnutrition. While these conditions occur frequently as part of the pellagra symptom-complex, rarely in association with beriberi, and in a wide variety of combinations, it is evident that each is separate, sometimes existing independently. The evidence at present available points to vitamin-B-complex deficiency as contributory to the causation of all these states, but only in the case of " burning-feet " syndrome is there any indication of the individual factor (pantothenic acid) which may be incriminated.

The chapters recording the author's personal experiences are outstanding and could have been compiled only on the basis of much acute observation and careful investigation. As Adviser in Neurology, Middle East Command, he had the opportunity of studying a wide range of deficiency-diseases among refugees and prisoners of war ; particularly a syndrome comprising retrobulbar neuritis, nerve-deafness and sensory ataxia. The general descriptions are supported by selected case-histories (in an appendix) and numerous illustrations.

The section dealing with nutritional neuropathies in prison-camps in the Far East suffers somewhat by comparison. It was, of necessity, based on a variety of reports, some very fragmentary, and important data were still unpublished at the time when it had to go to press. The resulting summary lacks the stamp of mature consideration which is apparent in the rest of the book.

Dr. Spillane has done great service both to nutritionists and neurologists in marshalling the facts and observations contained in this monograph. He has gone far to define the complex problems and indicate hopeful fields of investigation, not only of recognized nutritional neuropathies but of some nervous diseases in whose causation nutrition has not hitherto been generally thought to play a part.

Dean A. Smith

1177 Medical Disorders of the Locomotor System including the Rheumatic Diseases

Ernest Fletcher. Edinburgh, E. & S. Livingstone Ltd., 1947. xii + 625 pages ; 262 figures. £2 5s. [£2.25]

(i) Definition and classification of rheumatic diseases ; (ii) clinical examination of patient suspected of some locomotor disorder ; (iii) physiology of joints ; (iv) applied anatomy of locomotor system ; (v) incidence and prevalence of adult rheumatism ; (vi) predisposing conditions applicable in many forms of rheumatism ; (vii) focal infection ; (viii) laboratory findings in rheumatism ; (ix) radiology in arthritis ; (x) aetiology and pathology of rheumatic fever ; (xi) diagnosis and treatment of rheumatic fever ; (xii) chorea ; (xiii) the relationship of rheumatic fever and rheumatoid arthritis ; (xiv) aetiology of rheumatoid arthritis ; (xv) diagnosis of rheumatoid arthritis ; (xvi) treatment of rheumatoid arthritis ; (xvii) variants of rheumatoid syndrome ; (xviii) subcutaneous nodules ; (xix) skin manifestations in rheumatism ; (xx) aetiology and pathology of osteoarthritis ; (xxi) diagnosis and treatment of osteoarthritis ; (xxii) osteoarthritis of the spine ; (xxiii) aetiology and pathology of fibrositis—diagnosis and treatment of fibrositis ; (xxiv) specific arthritides ; (xxv) miscellaneous lesions ; (xxvi) ankylosing spondylitis ; (xxvii) medical diseases of bone ; (xxviii) gout ; (xxix) sciatica ; (xxx) brachial neuralgia ; (xxxi) the shoulder joint ; (xxxii) backache and the spine ; (xxxiii) the foot ; (xxxiv) peripheral vascular disorders ; (xxxv) physical therapy. Appendix I. Solutions used for injections. II. Manipulation—epidural injection—serial plasters. III. Technique of joint and muscle injections. IV. Optimum position for ankylosis. V. Muscle nerve testing. VI. Certain normal blood values. Index.

Books on the rheumatic diseases published during the nineteen-thirties used to be small, rather thin volumes, as befitted a subject about which little was known and less was cared. This 1947 book runs to 625 pages and invites comparison with another fairly recent " big " book on the subject, Comroe's *Arthritis*, containing 752 pages in the first (1940) edition. Both are disproportionately heavy, in relation to their length, compared with the pre-war publications, since they are printed on good-quality paper suitable for the reproduction of photographs and *x* rays. This increase in unwieldiness is not primarily due to any great advance in our knowledge of the cause of " rheumatism ", but rather to an increased knowledge of the things we do not know about it, and to a reluctance to discard those old bits of knowledge we now know are probably not so (e.g. the section on obesity). It is due also to the increased use of photographs and *x* rays in illustration, a practice which should add greatly to the readability of a book by diminishing the reading-matter. Both books are generously illustrated but contrast markedly in this respect : of Comroe's 200 illustrations, 191 were borrowed from other publications, whereas, of an even greater number in the book under review (262), the vast majority are original. Some slight duplication (e.g. fig. 12 and 187, 131 and 149, 162 and 230) might perhaps be eliminated in the next edition, together with the coloured pictures which show no more than plain ones would, but, on the whole, the illustrations are well chosen and excellently produced. A special tribute should be paid here to Dr. Golding, in whose chapter the *x*-ray photographs of digits are enlarged and trimmed to a size where it is possible to appreciate them visually instead of, as so often happens, through the eye of faith and the medium of the legend.

So much for the format. The contents, as may be seen from the chapter-headings listed above, cover a wide field. Particularly interesting are the specialist contributions, e.g. on dental infection by Calthrop, applied anatomy by Mitchell, radiology by Golding, electromyography by Weddell, etc. Dr. Copeman contributes a well-balanced account of fibrositis, and Dr. Donald Hunter an admirably brief (16 pages) but lucid and compact section on medical diseases of bone. The emphasis throughout the book is on clinical and therapeutic aspects : in contrast to Comroe's book, where original observations seldom intrude, this account is, in places, highly personal, quoting results of the author's own series and fragments of case-histories from a wide background of clinical observation. It is decidedly not a physiotherapist's handbook : many would feel that the value of active and passive exercises and movement was not sufficiently emphasized in the short chapter on physiotherapy, but full reference is made to this aspect under the treatment of the various individual diseases. A short bibliography, mainly anglo-american, is given at the end of each chapter, which could, in one or two instances, be lengthened to include all the authors mentioned in the text or at least one key-reference to each syndrome described. Six appendices on technical details of aspiration, injection, manipulation, etc., end a book which, it is thought, will prove both interesting and useful to those who deal with disorders of the locomotor system.

MEDICAL ADMINISTRATION AND PUBLIC HEALTH

1178 Law Relating to Hospitals and Kindred Institutions (incorporating "Law for Nurses")

S. R. Speller. London, H. K. Lewis & Co., Ltd., 1947. xxxv + 399 pages. 22 x 14 cm. £1 2s. 6d. [£1.125]

Index to cases cited. Table of statutes. Part I. (i) Introductory; (ii) hospitals—definition, and classification; (iii) constitution of hospitals; (iv) general powers of hospital authorities; (v) charitable trustees and the Charity Commissioners; (vi) provision of pay beds. Part II. (vii) Consents to operations and analogous matters; (viii) injuries to patients and others; (ix) detention of patient against his will; (x) persons of unsound mind and mental defectives; (xi) loss of or damage to patient's property; (xii) births and deaths in hospital; (xiii) professional confidence and cognate matters; (xiv) ownership of medical records; (xv) poisons and dangerous drugs. Part III. (xvi) Professional qualifications; (xvii) law of master and servant as affecting hospital staff; (xviii) statutory regulation of conditions of employment; (xix) hospital rates, taxes and duties; (xx) raising money for hospitals; (xxi) gifts by will to hospitals; (xxii) hospital charges; (xxiii) nuisance and trespassers. Part IV. (xxiv) Contracts; (xxv) sale of goods; (xxvi) insurance; (xxvii) cheques, money orders and postal orders; (xxviii) the nurse's contractual position; (xxix) nursing homes and agencies for the supply of nurses; (xxx) the Public Health Act, 1936, and the Public Health (London) Act, 1936. Part V. (xxxi) National Health Service Act, 1946. Bibliography. Index.

Mr. Speller has had much experience in the legal pitfalls which may beset the hospital worker. In addition to being a Barrister-at-Law, he is Secretary and Director of Education of the Institute of Hospital Administrators and Editor of *The Hospital*. A book from his pen deserves very careful attention.

The administration of hospitals and allied institutions covers almost the whole field of human relationships and, in consequence, touches at one point or another every branch of the law, including even some aspects of criminal law. In addition to the broad general powers and duties of hospital-authorities, there are the complex relationships between hospitals and their staffs and between the staffs and the patients. In addition, there are the many special aspects, for example the law relating to insurance; the implications of the Factories Acts; the Pharmacy and Poisons Act; the Workmen's Compensation Acts; the Road Traffic Acts, etc.

One of the main characteristics of the present century has been the increasing tendency of the central government to intervene, by Statute, with the personal health-services. The Lunacy and Mental Treatment Acts and the Mental Deficiency Acts have most important effects on hospital-administration. So also has the great consolidating Public Health Act of 1936. Clearly the Midwives Acts of 1902–1936 and the Nurses Act of 1943 have also profound effects on hospitals. But it is the social legislation of the past few years that is the most revolutionary in its results. The comprehensive treatment of schoolchildren under the Education Act of 1944, the National Insurance Act of 1946 and above all the National Health Service Act will, when carried into full effect, completely alter the present arrangements in Britain for medical care, and establish a comprehensive medical service for the whole nation. Much of the law so carefully set out by Mr. Speller in this book will, therefore, be superseded in the near future. This applies particularly to Part I dealing with the definition, constitution, and powers of hospital-authorities. After the appointed day under the National Health Service Act, the present law will relate to only a small minority of hospitals and institutions not included in the National Health Service. It is necessary, therefore, to read Part I in conjunction with Part V, which describes the National Health Service Act in detail. The author makes it clear that this book is not intended as a book of reference for the legal profession, but even so it has been necessary for him to deal in some detail with the legal principles underlying the various branches of the law. Part II of the book deals with the general relationship between the patient and the hospital, and is admirably set out and clearly written. This comment applies equally to the chapters in Part III dealing with professional qualifications and the Law of Master and Servant. While it is invaluable to be able to refer to these general principles, it must be remembered always that no-one can forecast the reaction of the Courts to the individual case. This is particularly well illustrated by the case of Gold v. Essex County Council (1942.2A.E.R.237) described on pages 92 and 93 of this book.

In 1940 the author published his *Law for nurses*. This is now revised and incorporated in the present work but, even so, the author makes it clear that he was in two minds whether to publish this book now or wait until the National Health Service had been in existence for a little while. He proposes to bring out a companion-volume later. It is a pity that the present volume could not be comprehensive, but enough has been said to show the great practical value of this work. The author has contrived to produce in compact form a clear exposition of the principles of the law relating to hospitals. Those who know anything of the complexities of english law and the revolutionary effects of the new social legislation will appreciate the difficulties with which he has had to contend.

A. Leslie Banks

1179 Municipal Health Services

Norman Wilson. London, George Allen & Unwin Ltd., 1946. 178 pages. 19 x 13 cm. 7s. 6d. [£0.375]

(i) Introduction. Part I. The services described. (ii) Maternity and child welfare; (iii) the health of the school child; (iv) tuberculosis and its treatment; (v) the control of communicable diseases; (vi) the care of the mentally afflicted; (vii) general hospitals; (viii) Poor Law and other services. Part II. The administrative machinery. (ix) The distribution of powers and duties; (x) local administration; (xi) the Ministries of Health and Education. Part III. A National Health Service. (xii) Medical services; other agencies; (xiii) need for an integrated service.

Here is a clear, brief but comprehensive account of the personal health-services. Within the 178 pages of this modestly-priced book, there is described in the first and main part services such as maternal and child-welfare, school-health, tuberculosis, control of communicable diseases, the care of the mentally afflicted, and the services provided by the general hospitals and the Poor Law. The second and third parts contain an excellent account of the administrative machinery involved, seen against the background of the needs and difficulty of local authorities.

Due doubtless to the delays and difficulties of publishing nowadays, it has not been possible to include an account of the import of the National Health Service Act on municipal health-services. This is most unfortunate, for if one requires an up-to-date and "near-future" description of our health-services, the omission is serious. Much of the present-day financial aspects of public health, the provision of free services, specialist services such as those for tuberculosis and venereal disease, abolition of compulsory vaccination, the school leaving-age—in all these and in many other matters, changes have already been determined by Parliament. Omission of any description of these changes inevitably lessens the value of this volume.

In these days of vast change, the task of an author is indeed difficult. The author of the volume under review has been particularly unlucky in this respect, for his able and valuable book *Public health services* was published shortly before the outbreak of war, when preoccupation with pressing duties of civil defence prevented the proper study and appreciation of a penetrating survey. The present volume contains reference to the disparities in the range and efficiency, in the quantity and quality of personal health-services offered by present local authorities to the citizen. In this aspect of the subject, the author has rendered outstanding service. Vigilance will be required to see that possible local inertia does not allow anything less than a uniformly-high standard of services throughout the country.

Personal health-services have been one of the glories of english social history of the last 100 years. The author tells with a compact lucidity the grand story of the development of these services, with mention of the great names of Chadwick, Simon, Ballantyne, Robert Philip, Florence Nightingale and the MacMillans. In this field, Britain has led the world. It must be admitted that we have been recently overtaken in some services, but we look to opportunities afforded by the operation of the National Health Service Act to regain a clear lead.

Every chapter of the present volume shows an exact knowledge of public health services in theory *and* in practice, as well as a sympathy with the common people in their needs, and deep insight into the problems involved in the provision of these services.

J. L. Burn

1180 Preventive Medicine and Public Health

Wilson G. Smillie. New York, The Macmillan Company, 1947. xvi + 607 pages; 41 illustrations. 22 x 15 cm. £1 10s. [£1.5]

Section I. Introduction. (i) Introduction; (ii) population trends and the public health; (iii) vital statistics. Section II. Environmental sanitation. (iv) Introduction: importance of sanitation of the environment; (v) water supplies and swimming pool sanitation; (vi) excreta disposal; (vii) vermin and their control; (viii) fumigation and disinfection; (ix) food inspection; (x)

sanitation of milk, and milk as a transmitter of disease ; (xi) disease transmitted through food other than milk and milk products (food poisoning) ; (xii) the general environment in relation to health and disease ; (xiii) housing and its relation to health. Section III. Communicable disease control. (xiv) General principles of communicable disease control ; (xv) epidemiology ; (xvi) control of communicable diseases of childhood ; (xvii) control of acute respiratory infections ; (xviii) control of enteric infections ; (xix) control of tuberculosis and leprosy ; (xx) venereal diseases : their prevention and control ; (xxi) control of the rickettsial diseases ; (xxii) control of a miscellaneous group of infectious diseases. Section IV. Child hygiene. (xxiii) Child health protection ; (xxiv) oral hygiene ; (xxv) school health services. Section V. Adult health protection and promotion. (xxvi) Geriatrics ; (xxvii) mental hygiene ; (xxviii) malnutrition and its prevention ; (xxix) control of cancer ; (xxx) preventive aspects of peptic ulcer and appendicitis ; (xxxi) the role of public health and preventive medicine in heart disease and hypertension ; (xxxii) preventive aspects of obesity and diabetes ; (xxxiii) preventive aspects of arthritis ; (xxxiv) preventive aspects of allergic conditions ; (xxxv) preventive aspects of alcoholism ; (xxxvi) industrial hygiene. Section VI. Public health administration. (xxxvii) Administration of local health services ; (xxxviii) rural health administration ; (xxxix) municipal health administration ; (xl) state health administration ; (xli) national health services ; (xlii) voluntary health activities ; (xliii) health education ; (xliv) the public health nurse ; (xlv) medical social work ; (xlvi) adequacy of medical care ; (xlvii) a nation-wide medical care program. Index.

This book has been prepared for american medical students " . . . . who are planning to practice clinical medicine, and who are interested primarily in the diagnosis and treatment of disease ", and the prospective reader, attracted by its title, would do well to bear this in mind when glancing through the list of contents. The work is chiefly concerned with preventive medicine as an essential part in the practice of clinical medicine, and with the duties and obligations in this field of the individual physician to his individual patients. We are not surprised therefore that the author, in his chapter on Child Health Protection, gives prematurity as the principal cause of neonatal deaths without making any direct reference to the causes of the cause (in the socio-economic background of the pregnant woman), while he devotes a page to the care of the premature infant and almost as much space to the etiology of erythroblastosis foetalis. The author's thesis is that the essential difference between Public Health and Preventive Medicine rests in the allocation of responsibility for carrying out the necessary activities involved. The former is a community-responsibility while the latter is the responsibility of the individual and his family. It is to the general practitioner in his role of medical adviser to that individual and his family that this work is directed. Even in these days of increasing health-consciousness, however, the general practitioner is still largely concerned with morbidity and the author is obliged to approach individual and public health from this starting-point. In spite of the limitations imposed upon him by the nature of his text, one would have liked to see the author use his undoubted flair for lucid exposition to greater advantage in emphasizing the need for a more positive approach to the problems of individual and communal health.

A pleasing feature of the book is the graphic and effective use of actual clinical material by way of illustration of the more important points throughout the text. The section on communicable disease is particularly well done though one is surprised, in passing, to see no reference to the association of congenital defect and rubella in this recently-published work.

Students in Britain will be particularly interested in the two last chapters in which the author discusses existing medical services in the USA and the pros and cons of a national comprehensive medical service (to which he is emphatically opposed). Just as the public-health aspects of malnutrition differ in the USA from those in Britain (" The difficulty is that we fail to utilize readily available foods." p. 411), so also does a national comprehensive medical service present different problems in the two countries according to the peculiar historical, social and economic forces at work, however much the general principles apply to both.

R. S.

MICROSCOPY

1181 The Microscope. Its Theory and Applications

J. H. Wredden. London, J. & A. Churchill Ltd., 1947. xxiv + 296 pages ; 298 illustrations. 25 x 15 cm. £1 1s. [£1.05]

(i) Historical introduction by W. E. Watson-Baker; (ii) elementary optics; (iii) the compound microscope; (iv) the eyepiece; (v) the objective; (vi) the substage condenser; (vii) illumination; (viii) the stand and mechanical parts; (ix) the use of the microscope; (x) an introduction to the polarising microscope; (xi) micrometry; (xii) photomicrography; (xiii) the preparation of specimens. Appendix: Refractive indices, conversion tables, useful constants, properties of circles and spheres, Nobert's test plate rulings, logarithms and anti-logarithms, natural sines. Index.

The microscope has by now become an indispensable tool in laboratories, factories and workshops: inevitably many of those who are called upon to use it have little or no knowledge of the theory of optics, and too frequently perhaps only a perfunctory knowledge of what is essentially a precision-instrument. Mr. Wredden's book is admirably designed for those who, with but slender acquaintance with optics, are anxious to know how to use the microscope to the best advantage. Even experienced microscopists, however, will find much of interest and instruction in its pages. The appearance of such a work at the present time is particularly opportune, for microscopes, like so many other things, are scarce and much damage may easily be done to so sensitive an instrument by careless or ignorant handling.

The first part of the book is rightly allotted to the theoretical principles of optical instruments, and to the application of these principles in the mechanical construction of the microscope. Unless these are firmly grasped at the outset, there is no sure foundation on which more extensive knowledge can be built. A brief historical introduction is contributed by W. E. Watson-Baker, who deals with the main developments in optical instruments from the time of Roger Bacon onwards, particular attention being paid to features of the microscope so often neglected—such as stand, mechanical stage, substage and accessory apparatus.

The question of the optical system of the microscope is then taken up, refraction, the lens, chromatic aberration and image-formation being described with the help of simple diagrams. Having examined the principles of the simple microscope and the way in which magnification is produced, the arrangement of the compound microscope is discussed. Each of the various components is fully described, the section on resolution being particularly instructive. If the instructions on the use and care of objectives were more fully known, there would be far fewer complaints of the deterioration of lenses. A note might well be added in a future edition on how to prevent fungus-growth on lenses in warm climates, a discovery which in the late war saved many thousands of pounds worth of precious optical apparatus.

In connexion with substage condensers, the whole question of paraboloid condensers is very fully discussed, again with diagrams, while the section on dark-ground illumination is highly commendable. Critical illumination is a subject which is far too often neglected despite the fact that its principles were clearly demonstrated by that great english microscopist, E. M. Nelson, who died in 1938.

There are few books which give more useful tips both on the care of the instrument and, what is too often completely overlooked, the care of the microscopist's eyes—an essential but neglected link in the formation of a true visual image.

The polarizing microscope is adequately dealt with together with micrometry and projection-apparatus. A section on photomicrography includes details of the author's own apparatus for producing a critical image on the viewing-screen of the camera.

The book closes with a short sketch of methods for preparing sections and, in appendices, with a series of important tables dealing with refractive indices, conversion-factors from microns to fractions of an inch, and kindred subjects. The majority of the chapters provide references for further reading : many of these references are unsatisfactory, since they fail in the case of books to indicate the year of publication or the edition referred to, while in the case of periodicals the year, volume and page are omitted. In a second edition, reference might well be made to the use of ultra-violet radiation as an illuminant, to phase-microscopy, and even to the electron-microscope.

G. M. Findlay

PSYCHOLOGICAL PROBLEMS OF AERIAL WARFARE

1182 Psychological Disorders in Flying Personnel of the Royal Air Force Investigated during the War 1939–1945 (Air Ministry Publication 3139)

By various Authors. London, His Majesty's Stationery Office, 1947. iii + 344 pages ; 5 figures. 24 x 14 cm. 7s. 6d. [£0.375]

(i) Critical review of the published literature; (ii) use and abuse of the term " flying stress "; (iii) series of cases with psychological disorder examined in relation to the problem of selection of flying personnel; (iv) personal investigation of psychological disorder in flying personnel of Bomber Command; (v) personal

investigation of psychological disorder in flying personnel of Fighter Command; (vi) personal investigation of psychological disorder in flying personnel of Coastal Command; (vii) investigation of psychological disorder in flying personnel by the unit medical officers; (viii) human response to flying stress (based on the Dunham and the Croonian Lectures for 1943); (ix) statistical survey of the occurrence of psychological disorder in flying personnel in six months (3rd February to 3rd August, 1942); (x) clinical and statistical study of neurosis precipitated by flying duties; (xi) occurrence of neurosis in Royal Air Force (air crews), 1943-1944; (xii) occurrence of neurosis in Royal Air Force (air crews), 1944-1945; (xiii) time of recognition of neurosis in flying personnel; (xiv) predisposition to psychological disorder in normal flying personnel: (xv) signs of temperamental unsuitability in air crews under training. Appendix to chapter xv. Notes for flying instructors on recognition of nervousness in pilots under training; (xvi) assessment of temperament in connection with selection of air crews: the psychiatric method employed. Appendix to chapter xvi: Note on the observers' analysis of their method; (xvii) probability of return to full flying of men who have broken down under the strain of operational duties; (xviii) prognosis for a return to full flying duties after psychological disorder; (xix) some measures of the effect of operational stress on bomber crews; (xx) episodes of unconsciousness, confusion and amnesia while flying; (xxi) psychological aspects of airsickness; (xxii) reliability of psychiatric opinion in the Royal Air Force; (xxiii) fluctuations in navigator performance during operational sorties. Glossary. Index.

These studies were carried out in circumstances which made leisurely experiments and well-controlled observations practically impossible, yet they show a consistently high level of thoroughness and sound judgement in seizing on essential problems and making the most of the available data. The bulk of the papers was submitted between 1942 and 1944 to the Flying Personnel Research Committee, and all but four of them were the work of Air Vice-Marshal Sir Charles Symonds and Wing-Commander Denis Williams.

The strain to which RAF aircrews were exposed made it imperative that psychological disorders should be promptly detected and, to the fullest extent possible, prevented. Consequently the nature and causes of these psychological disorders needed close investigation. The first six chapters of this book, written during 1942, show how methodically this was done. The published literature is critically reviewed, the concept of " flying stress " as an illness in itself is examined (and rejected), and a preliminary study is made of 100 members of aircrew referred on account of neurotic symptoms, with a particular eye to evidence of predisposition which might have been detected at the time when they were selected for air-duties. Then the experience of executive and medical officers is tapped to discover the causes and signs of psychological upset in aircrews of Bomber, Fighter and Coastal Commands. The Croonian Lectures in 1943 provided the occasion for a review of some general and theoretical implications of the evidence of fear, courage, and emotional tension exhibited by flying personnel ; in these lectures the concept of inhibition is borrowed from neurophysiology, and elaborated along Pavlovian lines, though unfortunately the circumstances in which the lectures were delivered prevent detailed consideration of the difficulties inherent in such interpretation.

A series of papers analyzing the incidence of various forms of psychological disorder in the aircrews led to a more and more emphatic statement of the importance of predisposition : thus it was found that two-thirds of the flying personnel referred to neuropsychiatrists during a period of six months had been subjected to only slight flying-stress or none at all ; there was an inverse relationship between the signs of previous severe predisposition and the degree of flying-stress in these men. Such considerations as these showed the basic identity of the problems arising among airmen and the kindred problems familiar in civil life, the differences being only " in the kind and degree of psychological stresses encountered, which in turn depend upon the specialised and hazardous nature of the patients' duty."

The study of predisposition in aircrew who have broken down casts the problem back to the means of detecting predisposed men at the stage of selection and preliminary training. Chapters 15 and 16 deal with the psychiatrists' data on this, collected in an investigation of 1009 pilots under training and 335 night-bomber pilot-instructors who had completed their tour of operational duty : an interview was the basis for determining the presence of any of ten specified traits considered to be indicative of predisposition, and for rating the degree of predisposition in the individual pilot. The conclusions indicate, *inter alia*, that such traits as anxiety, obsessional features and a family history of mental illness could be found in pilots who completed their operational tour without needing psychiatric attention, whereas timidity, lack of persistence, affective lability and psychological immaturity were associated with severe predisposition to breakdown. An investigation such as this relies heavily on the acumen of the psychiatrist: hence the need for the interesting chapter, by Professor Bradford Hill and Wing-Commander Williams, which examines the reliability of psychiatric opinion, as judged by the agreement found between reports on the same man by different psychiatrists. An incidental observation arising from the latter inquiry was that in many cases there can, from the medical aspect, be no certain dividing line (such as is commonly assumed) between normal and abnormal fear, i.e. anxiety. Prognostic and statistical papers, by Squadron-Leader D. D. Reid, report various measures of the effect of stress, and, with clinical studies on airsickness and episodes of unconsciousness, make up the rest of this very informative work.

A. J. L.

SUPPORT FOR THE IMPOTENT

1183 The Treatment of Impotence. With special reference to Mechanotherapy

Joseph Loewenstein. London, Hamish Hamilton Medical Books, 1947. 49 pages ; 4 figures. 19 x 12 cm. 6s. [£0.3]

(i) Introduction; (ii) definitions; (iii) physiological mechanism of erection; (iv) psychological impotence and psychological treatment; (v) history and literature of mechanotherapy; (vi) the technique of the C.T.A. treatment; (vii) the course of the C.T.A. treatment; (viii) indications; (ix) statistics; (x) failures of mechanotherapy; (xi) mechanotherapy and fertility; (xii) case records. References. Index.

Functional impotence may respond rapidly to treatment or it may prove refractory to even a long course of psychotherapy. Any ancillary method of treatment which will allow of the patient's achieving an even moderately successful sexual intercourse is therefore invaluable, since it will restore what has so far been lacking, namely, confidence in his sexual capacity. The author of this book has called attention to a method of treatment which has fallen into disuse in Britain. Krafft-Ebing was of the opinion that mechanical expedients will always be in demand in the treatment of impotence, but in England the use of penile splints is almost unknown. This is probably due to the fact that an easily adjustable mechanical support for the penis has hitherto not been available. Dr. Loewenstein has supplied what we have lacked and his " coitus training apparatus " should be of great use both to psychologists and genitourinary surgeons. The technique of the use of this apparatus is of considerable importance and he gives a full account both of the method of applying it and of the measurements required in order to obtain a model of the right size. During the last four years he has treated 40 cases with his form of penile splint and has obtained 26 cures, the average duration of treatment being four months. As Dr. E. B. Strauss points out in his foreword : " Unsuccessfully treated impotence can be one of the most distressing conditions from which a man may suffer, with far-reaching effects not only on his own life but on the life of his dependents . . ." Any method of treatment which reduces the percentage of failures is therefore to be welcomed, and Dr. Loewenstein must be thanked for bringing again to our notice a remedy which has been forgotten. He writes simply and clearly and his text is supplemented by helpful illustrations.

Kenneth Walker

SURGERY AND OBSTETRICS

1184 Textbook of Surgical Treatment Including Operative Surgery

Edited by *C. F. W. Illingworth.* Third Edition. Edinburgh, E. & S. Livingstone Ltd., 1947. xii + 644 pages ; 289 illustrations. 25 x 16 cm. £1 12s. 6d. [£1.625]

(i) Pre-operative and post-operative care; (ii) wounds and wound infections; (iii) penicillin in surgery; (iv) the treatment of burns; (v) amputations; (vi) affections of blood vessels; (vii) affections of the skull and brain; (viii) affections of the spine and spinal cord; (ix) peripheral nerve injuries; (x) surgery of the autonomic nervous system; (xi) diseases of bones; (xii) diseases of joints; (xiii) tuberculosis of bones and joints; (xiv) paralysis and contracture; (xv) fractures; (xvi) affections of the shoulder region and arm; (xvii) affections of the elbow; (xviii) affections of the hand; (xix) affections of the hip; (xx) affections of the knee; (xxi) affections of the foot; (xxii) radiotherapy; (xxiii) plastic surgery; (xxiv) affections of the face, mouth, jaws, and salivary glands; (xxv) affections of the neck; (xxvi) affections of the thyroid gland; (xxvii) affections of the larynx, pharynx, and oesophagus; (xxviii) affections of the breast; (xxix) affections of the thorax; (xxx) hernia; (xxxi) affections of the stomach and duodenum; (xxxii) affections of the intestines; (xxxiii) affections of the rectum and anus; (xxxiv) affections of biliary tract, pancreas, and spleen; (xxxv) affections of the appendix; (xxxvi) affections of the kidney and ureter; (xxxvii) affections of the bladder and urethra; (xxxviii) affections of the male genital tract; (xxxix) rehabilitation. Index.

Good looks are always attractive, and this book certainly has the attraction of a good outward appearance. The saying that beauty is only skin-deep does not apply here, for the contents are also good, sound and well-presented. The fact that this is the 3rd

edition within four years suffices to show that the purpose for which the book was written—to present a general outline of surgical treatment for senior students—has been fulfilled.

The additions in this edition are supremely important, for that truly miraculous drug—penicillin—has been accorded its proper place in the treatment of carbuncle, osteomyelitis and the many other diseases for which it has proved so efficacious. There is also an excellent chapter describing the scope of its action and the dosage and technique needed for its administration.

The scope of surgery varies from year to year; in this book the addition of a chapter on rehabilitation is an illustration of this, and the entire absence of any reference to syphilis or gonorrhoea is perhaps another indication of the same fact. We think, however, that it might be worth while adding a short paragraph on glanders, anthrax and actinomycosis. Moreover, acute dilatation of the stomach ought to be mentioned, for this serious condition is often overlooked and needs further publicity than is usually accorded to it. The various contributors have shown a catholicity in their views and a moderation in expressing them so that we have little to criticize; we were however surprised to see on page 530 that with a volvulus of the sigmoid colon " . . . on no account must the distended colon be brought outside the abdomen", for we have continued to do this without ill effect for thirty years and cannot agree that it is wise to write: " . . . without the support of the abdominal wall it may rupture." If this accident has ever happened, such an exceptional occurrence surely ought not to be made the basis of a rule. Finally, we find it a little difficult to understand why the disorders of the mouth, pharynx and larynx are dealt with but no mention is made of that most important structure—the tonsil. However, this is a good book and we can recommend it to students.

V. Zachary Cope

1185 Introduction to Surgery

Virginia Kneeland Frantz & Harold Dortic Harvey. New York, Oxford University Press: London, Geoffrey Cumberlege, 1946. xii + 216 pages; 11 illustrations. 19 x 12 cm. £1 5s. [£1.25]

Introduction. (i) History; (ii) injury and inflammation; (iii) repair; (iv) degeneration, hypertrophy, atrophy, regeneration; (v) deformities; (vi) cysts; (vii) neoplasms; (viii) contusions; (ix) abrasions; (x) incised wounds; (xi) wounds with loss of substance; (xii) repair of accessory skin structures; (xiii) repair of mucous membrane; (xiv) repair of muscle; (xv) repair of tendon; (xvi) repair of hollow and solid viscera; (xvii) repair of nervous system; (xviii) repair of serous synovial surfaces; (xix) repair of cartilage; (xx) repair of bone; (xxi) foreign bodies; (xxii) calculi; (xxiii) infection; (xxiv) specific infections; (xxv) infection in serous and synovial cavities; (xxvi) infection in bone; (xxvii) drainage; (xxviii) operative wounds; (xxix) accidental wounds; (xxx) ulcers; (xxxi) burns; (xxxii) gangrene; (xxxiii) hemorrhage; (xxxiv) shock; (xxxv) contact with the patient; (xxxvi) surgical technique; (xxxvii) anesthesia; (xxxviii) plastic surgery; (xxxix) experimental surgery; (xl) l'envoi. Bibliography. Index.

This attractive little book is based upon an introductory course in second-year surgery at Columbia University—a course which Allen Whipple speaks of as " the most valuable and instructive course in the Surgical Curriculum ". It deals with the principles which underlie all surgical work, and certainly forms an excellent basis on which the student may build his own experiential superstructure. After a brief historical review, the authors deal with the pathology and clinical features of injury, repair, infection and inflammation as they affect different tissues and organs. Then ulcers, burns, gangrene, haemorrhage and shock are considered, and finally there is an excellent section on contact with and examination of the patient. In 208 pages there is compressed an immense amount of information, and after reading it through we consider it the most generally useful introduction to surgery we have yet seen. It is not entirely free from minor inaccuracies and omissions. A boil is not a simple abscess round a hair-follicle, but a small focus of infective gangrene; echinococcal cysts are not due to infection, for worms are not usually classed among the germs. We are told the way to prevent tetanus but not how to safeguard the patient against gas-gangrene. We think the authors go too far in saying that the " so-called pressure points along the arteries which have been recommended in First Aid Manuals, are not useful to the surgeon." Finally, though we are in favour of stimulating the student's own observation, we think it is rather discouraging to the student to be told: " No authority in surgery can be accepted without question ". Taken at its face-value, that statement would make both teaching and learning extremely arduous or impossible. Nevertheless, we strongly recommend this book to the student and hope that it may be possible to reduce the price in the future.

V. Zachary Cope

1186 The Student's Handbook of Surgical Operations

Sir Frederick Treves. Eighth Edition, *revised by Cecil P. G. Wakeley.* London, Cassell & Company, Ltd., 1946. xi + 574 pages; 281 illustrations. 15s. [£0.75]

(i) Ligature of arteries; (ii) operations on nerves; (iii) amputations; (iv) operations on the bones and joints; (v) tenotomy, including operations for the division of contracted muscles, ligaments, and fasciae; (vi) plastic surgery; (vii) operations on the face, throat and neck; (viii) operations on the abdomen; (ix) operations on hernia; (x) operations on the urethra; (xi) operations on the scrotum and penis; (xii) operations on the rectum; (xiii) operations on the head and spine; (xiv) operations on the chest; (xv) treatment of varicose veins; (xvi) radium and its use in the treatment of cancer; (xvii) skin grafting. Index.

Here is an old friend rejuvenated. Rejuvenation is a more difficult operation than most of those described in the book, but in this case it has been done well, though not perfectly. In fact, it is doubtful whether any senior surgeon can ever entirely put himself in the position of a student. There is something to be said for the revision of old books by young men of registrar status, for they alone know exactly what the students need.

In this edition, the reviser has eliminated much obsolete material and added some operations of recent growth. Gone are Lisfranc's, Tale's and Chopart's amputations, disregarded are Pirogeff's, Stokes-Gritti's, and Carden's, but we are rather glad to see that Syme's amputation still has a place in a student's manual. Ligature of the patent ductus arteriosus and lobectomy are described, and additions have been made to the section on neurosurgery. But we look in vain for any reference to the spleen, nor is there any description of laryngectomy or tonsillectomy, although we are told how to do a laryngotomy and how to open a peritonsillar abscess. It is strange that in the discussion of anaesthesia for thoracic empyema no mention is made of local anaesthesia, for that is in many cases the method to be chosen. In the section on nephrectomy we find no description of the technique so commonly employed in which clamps are placed on the renal pedicle. These few criticisms will show that there are many points which will need attention in future editions, but nevertheless the book will still prove useful to the student and provide an introduction to what has now become a very comprehensive subject.

1187 Textbook of Obstetrics

Gilbert I. Strachan. London, H. K. Lewis & Co. Ltd., 1947. xi + 731 pages; 326 illustrations. 24 x 16 cm. £2 5s. [£2.25]

(i) The anatomy and physiology of reproduction; (ii) normal reproduction; (iii) the newborn child; (iv) the pathology of pregnancy; (v) complicated labour; (vi) the morbid puerperium; (vii) obstetrical operations; (viii) the casualties of childbirth; (ix) blood transfusion in obstetric practice. Index.

This book, which covers the whole of obstetrics, embodies, as the author says " . . . . the experience of many years of teaching and practice in this speciality " and " . . . the personal aspect of the matter has been stressed . . . " Therein lies the charm of this new and valuable contribution to obstetrics; it is clearly the work of one who knows his subject, and the profusion of good illustrations makes it a book from which the undergraduate can learn all that he requires.

There is much in the book which deserves praise, the emphasis on conservatism in the policy of " hands off " deserves mention, especially now that caesarean section is becoming so popular and often so unnecessary a solution for many obstetrical difficulties.

The author's conservative outlook has, however, led to the advocacy of certain statements and policies with which many will disagree. Thus his average pelvic measurements are presented in an old-fashioned way without any measure of the range, and with a figure for the true conjugate which is much too low. His advice of 10—14 days in bed after childbirth will be criticized by many, and he still recommends a low-protein diet in pre-eclampsia. There does not appear to be any mention of the value of a salt-poor diet in such cases. The section on inertia is especially good, and it was delightful to read his criticism of the over-emphasis on pelvic shape usually associated with the names Colwell and Moloy. His outright condemnation of forceps-delivery in inertia in the second stage is not justified now that it is known that it is the paralyzing effect of the anaesthetic on the uterus rather than the inertia which is the danger. Though there is a section on blood-transfusion there is no mention of the

importance of the " Flying Squad " to bring blood to the patient's home, and it is clear that the author considers that blood is often given unnecessarily.

In spite of any shortcoming that has been mentioned this is a carefully-compiled book that should be popular. No one could study it without being the wiser for it.

C. Scott Russell

1188 Postgraduate Obstetrics

William F. Mengert. London, Hamish Hamilton Medical Books, 1947. xv + 392 pages ; 123 illustrations. 23 x 14 cm. £1 5s. [£1.25]

Section I: Pregnancy. (i) The diagnosis of pregnancy; (ii) prenatal care; (iii) minor ailments of pregnancy; (iv) disease complications related to pregnancy; (v) intercurrent diseases unrelated to pregnancy; (vi) abortion and premature labor; (vii) abnormal pregnancy; (viii) antepartum hemorrhage—placenta previa and premature separation; (ix) sex hormones in pregnancy; (x) estimation of the bony pelvis. Section II: Labor. (xi) The conduct of labor; (xii) obstetric analgesia and anesthesia; (xiii) postpartum hemorrhage; (xiv) repair of tears; (xv) obstetric forceps; (xvi) cesarean section; (xvii) miscellaneous delivery operations; (xviii) anomalies of the expulsive forces; (xix) miscellaneous complications of labor. Section III: The puerperium. (xx) Management of the normal puerperium; (xxi) care of the newborn; (xxii) anomalies, injuries, and diseases of the newborn; (xxiii) puerperal infection; (xxiv) miscellaneous diseases and complications of the puerperium; (xxv) the follow-up examination; (xxvi) sterility; (xxvii) the emotional stresses of pregnancy; (xxviii) laboratory and technical procedures. Appendix. Nursing technics. Index.

The scope of this book is any disease or complication in the pregnant, parturient or puerperal woman, and in the newly-born child, such as might occur in the practice of a physician seeing maternity cases at the rate of fifty a year. Apart from a short chapter on sterility there is no gynaecology. As its title suggests, this book is essentially a book for the practising physician ; it is pleasantly short, well written, covers a wide field, is sensibly illustrated and is up-to-date.

The author's attitude to many of the practical problems in obstetrics is so kindly, logical, and wise that the book might almost be described as excellent if it were not for a rather unjustified and recurring undercurrent of fear—the fear of caesarean section in the presence of sepsis. Thus, he doubts whether the operation should be performed after twelve hours of labour for fear of infection and insists that " . . . cesarean section in the presence of actual, and often with potential, infection is best followed by hysterectomy ", and that " cesarean section has little place in the treatment of prolonged labor due to uterine inertia. By the time prolongation of labor is recognized, twenty-four or more hours have elapsed. *Cesarean section late in labor imposes a prohibitive maternal mortality risk* unless the physician is prepared to perform extraperitoneal section or cesarean hysterectomy." Such an attitude must of necessity in some cases lead to the unnecessary performance of the operation early in labour, and before the uterus has been given a real chance of expelling its contents. Furthermore, it is not true ; with penicillin and sulphonamide-therapy the risk of caesarean section to the mother *even in the presence of infection* is not nowadays sufficient to withhold this line of treatment if the other circumstances of the case demand it.

This criticism should not lessen the general excellence of a book which I can thoroughly recommend to the practitioner who wishes to bring his knowledge of obstetrics up to date.

C. Scott Russell

1189 A Short Textbook of Midwifery

G. F. Gibberd. Fourth Edition. London, J. & A. Churchill Ltd., 1947. viii + 563 pages ; 195 illustrations. 21 x 14 cm. £1 1s. [£1.05]

(i) The anatomy of the pelvis and its contents; (ii) the development of the ovum; (iii) the anatomy and physiology of pregnancy; (iv) the diagnosis of pregnancy; (v) the management of normal pregnancy; (vi) the anatomy and physiology of normal labour; (vii) clinical course and management of normal labour; (viii) occipito-posterior positions of the vertex; (ix) multiple pregnancy; (x) ectopic pregnancy; (xi) pregnancy complicated by pelvic abnormalities; (xii) diseases of the ovum in the early months of pregnancy; (xiii) diseases of the ovum in the later months of pregnancy; (xiv) the toxaemias of pregnancy; (xv) diseases associated with pregnancy; (xvi) malpresentations; (xvii) presentation and prolapse of the cord; (xviii) contracted pelvis; (xix) abnormalities in uterine action during labour; (xx) abnormalities in the birth-canal during labour; (xxi) ante-partum haemorrhage; (xxii) abnormalities in the third stage of labour; (xxiii) the normal puerperium; (xxiv) puerperal infections; (xxv) the abnormal puerperium; (xxvi) obstetric operations; (xxvii) the normal infant; (xxviii) the premature infant; (xxix) the abnormal infant. Index.

This short textbook, now in a fourth edition, is firmly established as a good friend of the student and its popularity is well deserved ; it is clearly written, reasonably short and accurate and adequately illustrated. In one or two respects, however, it might be improved.

Thus the chapter on Puerperal Infections is rather too long and complicated. The description of the Management of the Primiparous Breech Delivery is lacking in just that detail which is so necessary for the successful conduct of such cases. In some respects, the author is over-conservative ; he believes that pyelitis of pregnancy should be treated with alkalis rather than with the sulphonamides, and in the section where he discusses upper-segment and lower-segment caesarean sections, he advises " that it is probably better to perform an upper segment operation if the patient is not in labour ". Although this advice may be suitable for the occasional operator, it is not in keeping with the trend of modern opinion. In the section on Contracted Pelvis, too much emphasis is placed on the size of the pelvis and too little on the size of the foetal head.

Apart from such relatively minor faults, the book is up-to-date, the text has been thoroughly revised and makes a useful contribution to the teaching of obstetrics.

C. Scott Russell

TROPICAL MEDICINE

1190 The Principles and Practice of Tropical Medicine

L. Everard Napier. New York, The Macmillan Company, 1946. xvi + 917 pages ; 24 plates ; 195 figures. 25 x 16 cm. £1 15s. [£1.75]

(i) General considerations; (ii) measures for mitigating the effects of tropical climate; (iii) diseases due to the direct effects of tropical climate; (iv) malaria; (v) leishmaniasis; (vi) trypanosomiasis; (vii) the relapsing fevers; (viii) rat-bite fever; (ix) leptospirosis; (x) the typhus fevers; (xi) oroya fever, or bartonellosis; (xii) yellow fever; (xiii) Rift valley fever; (xiv) dengue sand-fly group; (xv) plague; (xvi) tularaemia; (xvii) the undulant fevers; (xviii) melioidosis, (xix) the intestinal fluxes; (xx) leprosy; (xxi) yaws and associated diseases; (xxii) tropical skin ulcerations; (xxiii) lymphopathia venereum; (xxiv) granuloma venereum; (xxv) some common skin diseases of the tropics; (xxvi) helminthic infections; (xxvii) cosmopolitan intestinal nematode infections; (xxviii) tropical intestinal nematode infections; (xxix) tapeworm infections; (xxx) trichinosis; (xxxi) filariasis; (xxxii) dracontiasis, or guinea-worm disease; (xxxiii) gnathostomiasis; (xxxiv) schistosomiasis; (xxxv) other fluke infections; (xxxvi) hydatid disease; (xxxvii) nutrition and nutritional disorders in the tropics; (xxxviii) anaemia in the tropics; (xxxix) snakes and snake-bite; (xl) rabies; (xli) a note on myiasis and scarabiasis. Subject index. Author index.

This is a sound and readable book written in a vigorous clear style. The emphasis is laid mainly on tropical disease as seen in India, and in most chapters the author's wide personal experience gives peculiar vitality to his writing. The book has been written mainly for clinicians, but covers the parasitological, pathological and preventive aspects of the subjects discussed. There are certain unusual and strong-minded omissions. Smallpox and typhoid fever, for example, both of acknowledged importance in tropical countries, are not described, on the grounds that they are adequately dealt with in ordinary textbooks of medicine. Tuberculosis, eye-diseases and general mycotic infection are also excluded. On the other hand, space is given to an account of tularaemia. The author defends his " errors " of " omission and commission " in his preface.

The general arrangement of the book has gained considerably by skilful reduction to a minimum of those descriptions of arthropod vectors and laboratory procedures which so often make such volumes unwieldy. Each chapter is headed by an outline of its contents, an innovation likely to appeal to student-readers. The line-illustrations are clear, but some of the half-tone plates are indistinct and could be omitted without serious loss to the text.

The introductory chapters cover general considerations of life in the tropics, including a short account of the effects of heat. Some 70 pages are devoted to malaria, and make good reading. The clinical account is particularly clear, but certain points in the treatment of malaria are not altogether in keeping with contemporary views. The author refers several times to suppressive dosage with antimalarial drugs as " prophylactic " dosage, although he points out elsewhere that the process is one of suppression and not prophylaxis. He recommends the use of mepacrine [atebrin] as a " prophylactic " for an individual touring an endemic area, and quinine, rather than mepacrine, for a resident in such an area, " . . . in view of our lack of knowledge of the effects of atebrin over a very long period . . . ". He also suggests the use of 100 mg. mepacrine three times daily for 5 days in the treatment of benign tertian malaria and for 7 days (" but not longer ") in the treatment of malignant tertian. Later in the chapter he details the higher

dosage of mepacrine used during the war by the US Army, and recommends "For causal prophylaxis (suppressive treatment), the daily administration of 0.1 gramme of atebrin for six days a week . . .".

Professor Napier has added this and similar summaries of recent information to the text of the first half of the book in an attempt to bring up to date the earlier chapters, which, as he explains in a footnote in the preface, were published separately in India in 1943. This is understandable in view of the enormous volume of work done during the war and only now being released for publication, but such addenda sometimes lead to confusion, especially when the information they contain is at variance with that in the main text. The brief chapter on blackwater fever suffers in this way from a short addendum which modifies the text and serves to confuse the reader. For instance, the author recommends in the text the free use of alkali in the treatment of blackwater fever since ". . . at all costs the urine must be kept alkaline to prevent precipitation of the haematin and the consequent damage to the renal tubules." In the addendum to the chapter, however, he presents the more modern view that ". . . treatment by excessive alkalinization may do more harm than good." To the physician faced with a case of blackwater fever in which the kidneys are damaged and the urine remains persistently acid in spite of alkali treatment, these two statements are incompatible. The reviewer feels that on points such as this, the author should state his views clearly and definitely, as a guide to the reader; summaries of recent work are insufficient. No doubt this minor defect in this otherwise excellent book will be rectified in subsequent editions.

The chapters on kala-azar, leishmaniasis and cholera are first-rate. The author's wide personal experience dominates the picture and the result is a clear and precise account of both clinical and scientific aspects of the disease discussed. Helminthic infections are dealt with in an excellent series of chapters, and there are good chapters on trypanosomiasis, the relapsing fevers, rat-bite fever, Rift Valley fever, dengue, plague, undulant fever, melioidosis, the intestinal fluxes, leprosy (written by Dr. John Lowe), yaws, tropical skin-ulcerations, lymphopathia venereum, skin-diseases and nutritional disorders in the tropics. Pinta and bejel are discussed with yaws. Rabies is described very briefly, and there is an interesting section on snakes and snake-bite. In the immediate treatment of the latter, multiple incision through the fang-marks is recommended without any mention of preliminary washing of the wound to remove dribbled venom. In the list of common african poisonous snakes *Bitis gabonica* should have been included

B. G. Maegraith

PARTICULARS OF BOOKS REVIEWED ELSEWHERE IN THIS NUMBER

The numerals in square brackets are the serial numbers of the articles in which these books are reviewed

[1121] Intelligence and Fertility. The effect of the differential birthrate on inborn mental characteristics

Sir Cyril Burt. London, The Eugenics Society and Hamish Hamilton Medical Books, 1946. 43 pages. 21 x 14 cm. 2s. [£0.1]

(i) Early investigations on selected groups; (ii) later investigations on unselected groups; (iii) relation between intelligence and size of family; (iv) geographical distribution of intelligence and family size; (v) estimating the amount of apparent decline; (vi) rate of decline in the country as a whole; (vii) alleged increase of mental deficiency; (viii) final conclusion. Appendix: On the meaning of intelligence.

[1123] Researches on Pre-Natal Life. Volume I

Sir Joseph Barcroft. Oxford, Blackwell Scientific Publications, 1946. xiii + 292 pages; 124 figures. 25 x 19 cm. £1 17s. 6d. [£1.875]

(i) The disposition of vessels in the placenta; (ii) crossing the placental barrier; (iii) the growth of the body and of its constituent parts; (iv) comparison of length and weight in twins; (v) the relative claims of the foetus and mother to available nutritive material; (vi) the blood volume in the foetal circulation and its distribution between the foetus and the placenta; (vii) transfer of blood from the placenta to the foetus at birth; (viii) water content of foetal tissues; (ix) basal oxygen consumption of tissues considered in terms of slices; (x) the output of the heart; (xi) blood pressure; (xii) the development of vascular reflexes; (xiii) the oxygen capacity of the blood; (xiv) the oxygen dissociation curve; (xv) acid-base equilibrium and CO_2 dissociation curves; (xvi) the oxygen in the umbilical vessels; (xvii) the carotid blood; (xviii) the circulation through the foetal chest—the venous side; (xix) the circulation through the arteries in the foetal chest; (xx) closure of the ductus arteriosus and foramen ovale; (xxi) the respiratory process; (xxii) the onset of respiratory movement. Appendices. Indices.

[1124] The Embryology of Behavior. The Beginnings of the Human Mind

Arnold Gesell in collaboration with Catherine S. Amatruda. London, Hamish Hamilton Ltd. [1947]. xix + 289 pages; 391 illustrations. 24 x 16 cm. £1 1s. [£1.05]

(i) The search for beginnings; (ii) birth and age; (iii) zygote and embryo; (iv) the genesis of behavior; (v) the archaic motor system; (vi) the growth of fetal behavior; (vii) breathing behavior; (viii) muscle tonus; (ix) electrotonic integration; (x) the fetal-infant; (xi) the circumnatal infant; (xii) the diurnal cycle of sleep and wakeness; (xiii) species and individual; (xiv) the dynamic morphology of behavior; (xv) the hierarchical continuum. A photographic delineation of behavior patterns and growth sequences. Appendix A. The investigation in outline. B. The developmental diagnosis of age. Selected references. Index.

[1125] História da Lepra no Brasil. Volume I. Períodos Colonial e Monárquico (1500–1889)

Heraclides-Cesar de Souza-Araujo. Rio de Janeiro, Imprensa Nacional, 1946. xiii + 559 pages; 40 illustrations. 31 x 23 cm.

(i) Da descoberta do Brasil até o fim do dominio espanhol (1500–1640); (ii) a situação do problema da lepra na época dos vice-reis (1640–1808); (iii) história do Hospital dos Lazaros do Rio de Janeiro de 1763 a 1808; (iv) introdução e expansão da lepra no interior do Brasil na época dos vice-reis; (v) progresso da profilaxia da lepra no reinado de D. João VI (1808–1821); (vi) actividades contra a lepra durante o reinado de D. Pedro I (1821–1831); (vii) o problema da lepra no periodo da regência (1831–1840); (viii) reinado de Dom Pedro II (1840–1889). Primeira parte (1840–1860); (ix) reinado de Dom Pedro II (1840 a 1889). Segunda parte (1861 a 1889). Bibliografia. Índice geral.

[1126] Bacteria in Relation to Domestic Science

C. E. Dukes. London, Geoffrey Cumberlege: Oxford University Press, 1947. viii + 240 pages; 1 plate, 9 figures. 19 x 12 cm. 12s. 6d. [£0.625]

(i) General characteristics of bacteria; (ii) bacteriology of the air; (iii) bacteriology of the soil; (iv) bacteriology of water; (v) bacteriology of milk; (vi) bacteriology of milk products; (vii) bacteriology of meat, fish and eggs; (viii) bacteriology of fruit and vegetables; (ix) bacteriology of alcoholic beverages, ginger beer and vinegar; (x) bacterial decomposition and decay; (xi) preservation of food by heat; (xii) preservation of food by cold; (xiii) preservation of food by drying, salt and sugar; (xiv) preservation of food by chemicals and by lactic fermentation; (xv) bacterial food poisoning in general; (xvi) food poisoning due to Salmonella bacteria; (xvii) food poisoning due to dysentery and cholera; (xviii) enteric fever; (xix) staphyloccocal and streptococcal food poisoning; (xx) botulism. Glossary. Index.

[1126] The Bacteriology of Spray-dried Egg with Particular Reference to Food Poisoning

By various Authors. London, His Majesty's Stationery Office, 1947. 66 pages. 22 x 15 cm. 1s. [£0.05] (Medical Research Council Special Report Series No. 260)

(i) The bacteriology of dried egg; (ii) salmonella infections of human beings associated with the consumption of dried egg; (iii) outbreaks of food poisoning of the toxin type following the consumption of dried egg; (iv) salmonella infection of pigs probably due to dried egg. General summary and conclusions. References. Appendix.

[1127] Molecules Against Microbes

E. S. Duthie. London, Sigma Books Ltd., 1946. 156 pages; illustrated. 19 x 13 cm. 6s. [£0.3]

(i) Microbes and disease; (ii) chemical structure of drugs; (iii) discovery of salvarsan; (iv) chemistry conquers tropical disease; (v) chemistry conquers tropical disease (continued); (vi) chemistry conquers bacteria; (vii) discovery and development of penicillin; (viii) the conquest of wound sepsis; (ix) chemotherapy in everyday medicine; (x) recent developments and future prospects. Some landmarks in chemotherapy. Reference tables. Glossary. Index.

[1127] The Road to Penicillin: A History of Chemotherapy

Margaret Goldsmith. London, Lindsay Drummond Ltd., 1946. 174 pages; 26 illustrations. 22 x 14 cm. 10s. 6d. [£0.525]

(i) Introduction; (ii) early groping; (iii) early middle ages; (iv) Fracastorius and Paracelsus; (v) Leeuwenhoek's "little animals"; (vi) chemical attacks against disease; (vii) Edward Jenner; (viii) the beginning of modern progress; (ix) Perkin's aniline-purple; (x) Joseph Lister; (xi) Louis Pasteur; (xii) Robert Koch; (xiii) Paul Ehrlich; (xiv) the new chemotherapy; (xv) Sir Alexander Fleming; (xvi) Sir Howard Florey. Bibliography. Index.

[1127] Miracle Drug. The Inner History of Penicillin

David Masters. London, Eyre & Spottiswoode, 1946. 191 pages ; 23 illustrations. 15 x 22 cm. 10s. 6d. [£0.525]

(i) The battle of germs ; (ii) Fleming finds the mould ; (iii) the mould keeps its secret ; (iv) the third attempt ; (v) the fourth attempt ; (vi) a vital decision ; (vii) a pinch of brown powder ; (viii) the miracle ; (ix) the chemists triumph ; (x) Florey seeks American aid ; (xi) the struggle for production ; (xii) back from the grave ; (xiii) saving the wounded ; (xiv) the crystals are found ; (xv) the final phase. Appendix. Index.

[1129] The Endeavour of Jean Fernel. With a List of the Editions of His Writings

Charles Sherrington. Cambridge University Press, 1946. x + 223 pages ; 27 illustrations. 22 x 14 cm. 16s. [£0.8]

Part I : The struggle and its aims. Part II : The earliest "physiology." Part III : Success and the close. Appendix : notes, etc. List of editions of the writings of Jean Fernel. Chronology of events. Index.

[1130] Report on Nutrition in Newfoundland

D. P. Cuthbertson. Dominions Office. London, His Majesty's Stationery Office, 1947. 87 pages. 24 x 15 cm. 1s. 6d. [£0.075]

Historical introduction. Personal observations: (i) general; (ii) incidence of signs of malnutrition; (iii) background conditions affecting health and nutrition; (iv) food consumption levels and recommendations for their improvement. Summary, discussions and recommendations. Labrador. Acknowledgements. Bibliography. Appendices.

[1131] Report of the Water Pollution Research Board : with the Report of the Director of Water Pollution Research, 1st July 1939 to 31st December 1945

Department of Scientific and Industrial Research. London, His Majesty's Stationery Office, 1947. iv + 78 pages ; 14 illustrations. 24 x 15 cm. 1s. 3d. [£0.0625]

Report of the Water Pollution Research Board. Report of the Director of Water Pollution Research. (i) Water ; (ii) sewage ; (iii) industrial waste waters ; (iv) polluting effects of sewage and industrial wastes : (v) other investigations. Appendix : publications during the period 30th June 1939 to 31st December 1945 arising out of the work of the Water Pollution Research Board.

[1131] The Story of Water Supply

F. W. Robins. London, Geoffrey Cumberlege, Oxford University Press, 1946. x + 207 pages ; 31 illustrations. 22 x 14 cm. 18s. [£0.9]

(i) Natural supplies ; (ii) the beginnings of conservation ; (iii) ancient ponds ; (iv) primitive wells ; (v) ancient irrigation ; (vi) the predecessors of the pump ; (vii) Palestine and the Phoenicians ; (viii) ancient Greece ; (ix) ancient Rome ; (x) the Roman empire ; (xi) Roman Britain ; (xii) holy wells ; (xiii) the dark ages ; (xiv) mediaeval water supplies—the monasteries ; (xv) mediaeval water supplies (continued) ; (xvi) old leats ; (xvii) kanats ; (xviii) well-heads and fountains ; (xix) conduits ; (xx) early America ; (xxi) water sellers and carriers ; (xxii) the New River Company ; (xxiii) water wheels and wood pipes ; (xxiv) water divining ; (xxv) the village well ; (xxvi) the parish pump ; (xxvii) the nineteenth century—and after. Index.

[1132] Treponematosis

Ellis H. Hudson. New York, Oxford University Press ; London, Geoffrey Cumberlege, 1946. iv + 116 pages. 24 x 16 cm. 12s. 6d. [£0.625]

(i) The parasite ; (ii) historical review ; (iii) studies in diagnosis ; (iv) the "syphiloids". Summary and conclusion. Bibliography.

[1133] The Evolution of Genetic Systems

C. D. Darlington. Cambridge, University Press, 1939, reprinted 1946. x + 151 pages ; 26 figures. 22 x 14 cm. 12s. 6d. [£0.625]

Preface. (i) Premises of genetics ; (ii) the substance of heredity ; (iii) sexual reproduction ; (iv) meiosis : pairing and crossing-over ; (v) meiosis : the process of assortment ; (vi) change of quantity : polyploidy ; (vii) change of position ; (viii) hybrids : diploid and polyploid ; (ix) change of proportion ; (x) the atom of genetics ; (xi) chromosome mechanics ; (xii) genotypic control ; (xiii) the mechanism of crossing-over ; (xiv) the biology of recombination ; (xv) the pursuit of hybridity ; (xvi) the permanent hybrid ; (xvii) the evolution of sex ; (xviii) sterility : the contradiction ; (xix) apomixis : the escape ; (xx) the integration of the cell ; (xxi) the evolution of heredity. Bibliography. Index.

[1133] Animal Genetics and Medicine

Hans Grüneberg. London, Hamish Hamilton Medical Books, 1947. xii + 296 pages ; 33 illustrations. 20 x 13 cm. £1 1s. [£1.05]

(i) Inherited diseases in general ; (ii) advantages and limitations ; (iii) some principles of developmental genetics ; (iv) central nervous system ; (v) central nervous system (continued) ; (vi) central nervous system (continued) ; (vii) central nervous system (continued) ; (viii) central nervous system (continued) ; (ix) central nervous system (continued) ; (x) the organ of hearing ; (xi) the eye ; (xii) the eye (continued) ; (xiii) endocrine organs ; (xiv) endocrine organs (continued) ; (xv) the blood ; (xvi) the blood (continued) ; (xvii) the skeleton ; (xviii) the skeleton (continued) ; (xix) the skeleton (continued) ; (xx) the digestive tract ; (xxi) the urogenital system ; (xxii) the skin ; (xxiii) serology ; (xxiv) disease resistance ; (xxv) conclusions. Bibliography. Author index. Subject index.

[1134] The Louse. An Account of the Lice which Infest Man, Their Medical Importance and Control

Patrick A. Buxton. Second Edition. London, Edward Arnold & Company, 1947. viii + 164 pages. 47 illustrations. 22 x 14 cm. 10s. 6d. [£0.525]

(i) The Anoplura or sucking lice; (ii) the anatomy of *Pediculus humanus*; (iii) the biology of *Pediculus humanus*; (iv) the medical importance of *Pediculus humanus*: (v) the control of lice; (vi) the crab louse (*Phthirus pubis*). Appendix. References. Index.

[1135] Medicine. Volume I : The Patient and his Disease

A. E. Clark-Kennedy. Edinburgh, E. & S. Livingstone, Ltd., 1947. xii + 383 pages. 24 x 16 cm. £1

(i) Body and mind; (ii) symptoms; (iii) symptoms and signs; (iv) heredity and environment; (v) reactions of the body and the mind; (vi) the nature of disease. Summary.

[1136] The Psychology of the Unwanted Child

Agatha H. Bowley. Edinburgh, E. & S. Livingstone Ltd., 1947. xi + 112 pages. 19 x 12 cm. 6s. [£0.3]

(i) The essentials of good personality development; (ii) the causes and effects of emotional rejection; (iii) a study of children in substitute homes; (iv) remedies and methods of readjustment; (v) some psychological aspects regarding the care of children in homes. Appendix. Suggestions for further reading. Glossary. Index.

[1137] Retinal Structure and Colour Vision

E. N. Willmer. Cambridge University Press, 1946. xii + 231 pages ; 5 plates ; 77 text-figures. 14 x 22 cm. £1 1s. [£1.05]

Foreword. Preface. (i) The structure of the retinal elements ; (ii) the function of the retinal elements ; (iii) the spectrum in terms of rod and cone sensitivity ; (iv) the C.I.E. colour chart and a possible interpretation ; (v) impulse frequencies in retinal nerve fibres and the perception of colour ; (vi) the trichromatic basis for colour perception, and the perception of colour at the fovea centralis ; (vii) certain aspects of colour-blindness. Addendum. General statement of the theory. References. Notes on the construction of the colour chart. Author index. Subject index.

[1137] Researches on Normal and Defective Colour Vision

W. D. Wright. London, Henry Kimpton, 1946. xvi + 383 pages ; 233 illustrations. 15 x 25 cm. £1 16s. [£1.8]

Part I. Introduction. (i) The visual organ and visual processes ; (ii) visual perception. Part II. The colorimetric equipment. (iii) The principles, design and construction of the colorimeter ; (iv) the operation of the colorimeter. Part III. The luminosity curve. (v) The spectral sensitivity of the fovea and extra-fovea in the Purkinje range ; (vi) luminosity measurements with very restricted fields ; (vii) the interpretation and application of the mixed scotopic-photopic luminosity curves. Part IV. Colour mixture. (viii) The principles of colour measurement on the trichromatic system ; (ix) the re-determination of the trichromatic coefficients of the spectral colours ; (x) the re-determination of the mixture curves of the spectrum ; (xi) the physiological implications of the colour mixture data ; (xii) some miscellaneous colour matching data. Part V. Discrimination. (xiii) The sensitivity of the eye to differences in saturation ; (xiv) the sensitivity of the eye to differences in hue ; (xv) the sensitivity of the eye to differences in chromaticity ; (xvi) the analysis of discrimination data ; (xvii) the effect of adaptation on the size of the discrimination step. Part VI. Adaptation. (xviii) The principles of binocular matching ; (xix) direct adaptation using white adapting stimuli ; (xx) direct adaptation using coloured adapting stimuli ; (xxi) the derivation of the spectral sensitivity curves of the three-response theory from adaptation experiments ; (xxii) indirect adaptation using white adapting stimuli ; (xxiii) the measurement of subjective brightness. Part VII. Defective colour vision. (xxiv) The nature, classification and incidence of defective colour vision ; (xxv) anomalous trichromatism ; (xxvi) dichromatism ; (xxvii) monochromatism ; (xxviii) the colour-blindness of the central fovea ; (xxix) the interpretation of colour-blindness data. Part VIII. The fundamental response curves. (xxx) The interpretation of colour vision phenomena in terms of the fundamental response curves. Index.

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Shorter Notices

Vitamine, Hormone, Fermente. Ein Buch für Ärzte, Biologen und Studierende

Rudolf Abderhalden. Dritte Auflage. Basel, Benno Schwabe & Co. Verlag, 1946. 250 pages. 22 x 15 cm. Sw. fr. 14.50

In the words of the author " the object of this book is to assess the present position in the vast field of vitamin- hormone- and enzyme-research". Throughout the work the close relationship which exists between members of the three groups of " biocatalysts " is emphasized. All the principal and some of the lesser-known substances are dealt with. Each chapter is divided into paragraphs headed as follows : properties, chemistry, physiology, methods of assay, occurrence, clinical use and available preparations. The two latter aspects are treated very briefly, attention being focussed on the physiology of the substance concerned. The author points out that he has ignored theories and speculations, however tempting, and has confined himself to facts alone.

This book should be of use to all who are interested in this rapidly-progressing field without being able to follow the course of research in detail. It is hoped that the physician, being acquainted with the physiological properties of the vitamin-, hormone- and enzyme-preparations he uses, will be a better judge of their therapeutic value, so that disappointments, which already tend to discredit certain aspects of this field, may be avoided.

I. J. L.

La linfogranulomatosis inguinal subaguda o cuarta enfermedad venerea

Enrique Alvarez Sainz de Aja. Madrid, Gráficas González, 1946. 70 pages; 8 figures. 19 x 13 cm.

This pamphlet is addressed not to specialists but to general practitioners who may encounter cases of lymphogranuloma inguinale in daily practice. The author deals with the questions of contagion, incubation, clinical manifestations, symptoms, diagnosis, treatment and prognosis. The pamphlet is illustrated by eight photographic plates.

Lo que todo el mundo debe saber sobre la sífilis

Enrique Alvarez Sainz de Aja. Madrid, Gráficas González, 1946. 67 pages. 19 x 13 cm.

This pamphlet is addressed to the general public and to young people in particular and describes in plain and simple language the clinical manifestations, symptoms and prognosis of syphilis in its various stages. The author gives valuable information and advice regarding treatment available.

101 Clinical demonstrations to nurses

Hamilton Bailey. Second edition. Edinburgh, E. & S. Livingstone Ltd., 1946. 136 pages; 137 illustrations. 21 x 14 cm. 10s. 6d. [£0.525]

This book comprises brief accounts of 101 common clinical conditions with accompanying illustrations, mostly in colour. It should prove a useful aid to any nurse whether working in the wards or outpatient department. Granted that the surgeon should take every opportunity of demonstrating clinical cases to the nurses who are assisting him, there will be many conditions of which the opportunity of demonstration will be lacking, and this book certainly helps to fill the gap.

The clinical descriptions are simple and concise, and the illustrations for the most part excellent.

Z. C.

Les septicémies à staphylocoques

M. Bariéty & H. Brocard. Paris, J.-B. Baillière, 1945. 252 pages. 24 x 16 cm.

This book on staphylococcal septicaemia opens with a brief historical account of the work done on the subject. This is followed by a full discussion of the etiology of the condition, subdivided under the headings : the microbe ; and the original focus of infection. The next part covers the clinical manifestations, subdivided into sections on hyperacute forms, acute forms, subacute forms, chronic forms, special forms in children and diabetics and forms associated with certain infectious diseases. Chapters on diagnosis, prognosis, pathology and pathogenesis follow. The final chapter deals with all aspects and types of treatment ; a section entitled " mycotherapy" is devoted to penicillin, and the chapter closes with concise indications to the practitioner as to the best method of treatment according to the type and severity of the infection. There is a bibliography of over 400 references, an index of authors quoted, and a subject index.

A. H.-S.

Practical methods for the microbiological assay of the vitamin B complex and essential amino acids

E. C. Barton-Wright. London, Ashe Laboratories, Ltd., [1947]. 58 pages. 7s. 6d. [£0.375]

The importance of the vitamins, if not of the amino-acids, in ensuring good health has become common knowledge. On the strength of their health-providing qualities, many food-products are purchased without question of their real vitamin-content. Under an order of the Ministry of Food, manufacturers of food-products must indicate the content in their products of certain of the vitamins. For this purpose speedy and precise methods of determination are essential. Microbiological methods of assay go a long way in fulfilling this purpose.

In his book, Dr. Barton-Wright gives details of microbiological assays of riboflavin, nicotinic acid, aneurin, biotin, pyridoxine and pantothenic acid and eleven essential amino-acids. This he does with clearness and simplicity, and he indicates carefully the precautions to be adopted with each method. In fact, few should have any difficulty in following his instructions. They might, however, have been prefaced by a few remarks on bacteriological technique for the benefit of those working with bacteria

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BOOK REVIEWS

Continued from page 277

[1138] Report of the Governing Body, 1947

The Lister Institute of Preventive Medicine. London, The Lister Institute of Preventive Medicine, 1947. 12 pages. 25 x 19 cm.

[1144] Una Epidemia de Peste Bubónica en el Siglo XVI

José Viñes Ibarrola. Pamplona, Editorial Aramburu, 1947. 133 pages. 21 x 14 cm.

(i) La peste en Pamplona ; (ii) una herejia sanitaria ? ; (iii) estudio medico de la peste bubónica en el siglo XVI ; (iv) epidemiologia ; (v) el factor social ; (vi) profilaxis ; (vii) comparación con la epidemia de Milan, de 1630 ; (viii) los actos religiosos en la profilaxis de la peste ; (ix) otras actuaciones complementarias.

[1145] The Renaissance and its Influence on English Medicine, Surgery and Public Health

Sir Arthur Salisbury MacNalty. London, Christopher Johnson, 1946 ; 30 pages ; 3 illustrations. 22 x 14 cm. 5s. [£0.25]

[1146] Doctors Differ. Five Studies in Contrast

Harley Williams. London, Jonathan Cape, 1946. 253 pages 8 illustrations. 20 x 14 cm. 12s. 6d. [£0.625]

Part I : Prologue. Part II : John Elliotson (1791–1868), his triumph and his defeat. (i) John Elliotson ; (ii) apprenticeship ; (iii) Cobbett's pupil ; (iv) medical teacher ; (v) the first mesmerist ; (vi) showing the world ; (vii) more experiments ; (viii) the opposition ; (ix) at 35 Bedford Square ; (x) Wakley gives judgment ; (xi) disgrace ; (xii) worshipping students ; (xiii) journalism to the rescue ; (xiv) surgeons and others ; (xv) Latin abandoned ; (xvi) James Braid ; (xvii) an honest man ; (xviii) was he right ? ; (xix) after Elliotson. Part III : Hugh Owen Thomas and the making of orthopaedics. (i) Rural healers ; (ii) young Dr. Thomas ; (iii) the bonesetters ; (iv) an agnostic's faith ; (v) the torch carried on ; (vi) enters the nurse ; (vii) orthopaedics is born. Part IV : James Mackenzie and William Osler. (i) James Mackenzie ; (ii) talent for research ; (iii) the highland boy ; (iv) heart troubles ; (v) heart medicine ; (vi) the young Osler ; (vii) Regius Professor ; (viii) Mackenzie moves to Harley Street ; (ix) the wise physician ; (x) research strenuous ; (xi) opposite prototypes. Part V : William Macewen and the story of the brain. (i) Lister and Macewen ; (ii) early brain knowledge ; (iii) mapping the brain ; (iv) the brain atlas ; (v) chest surgery ; (vi) professor of surgery ; (vii) Victor Horsley ; (viii) Guilielmus Superbus ; (ix) the brain in the future. Part VI : Robert William Philip and Edward Livingstone Trudeau. (i) Back to the Pyramids ; (ii) the Breton genius ; (iii) the marvellous Koch ; (iv) Koch's inspiration ; (v) fresh air ; (vi) fresh air in the city ; (vii) the forest healer ; (viii) the original clinic ; (ix) the medical statesman. Part VII : Epilogue : Rembrandt's picture.

[1147] The Rotunda Hospital 1745–1945

O'Donel T. D. Browne. Edinburgh, E. & S. Livingstone Ltd., 1947. xx + 296 pages ; 44 illustrations. 25 x 19 cm. £2 2s. [£2.1]

Part I. The first hundred years. Part II. The second hundred years. Part III. The struggle against puerperal fever. Part IV. Operative midwifery. Part V. Anaesthesia and gynaecology. Part VI. Eclampsia. Synopais. Index. Graph.

for the first time. To this might also have been added a note on the work still needed to be done on the basal media used in microbiological assays. However, Dr. Barton-Wright's book should stimulate many to explore the analytical uses of micro-organisms to the extent that they have been in the USA, and it may provide a basis for the standardization of microbiological assays of vitamins and other substances.

Übersicht der gebräuchlichen und neueren Arzneimittel für Ärzte, Apotheker und Zahnärzte

E. Bernoulli & J. Thomann. Sechste neu bearbeitete Auflage. Basel, Benno Schwabe & Co. Verlag, 1946. xii + 568 pages. 18 x 12 cm. Sw. fr. 13.50

As pointed out in the foreword to this swiss materia medica, "For many doctors modern therapy means the prescription of proprietary drugs." Accordingly, the less-expensive pharmacopoeial forms of proprietary drugs are given wherever possible. Where it has been necessary to choose among proprietary drugs, preference has been given to those more readily available in Switzerland at the time this survey was made. Remedies are grouped comparatively, under the main headings of substances acting on the nervous, circulatory, respiratory, digestive and genito-urinary systems, and those affecting metabolism, infectious diseases, skin and mucous membrane. The concluding sections of this convenient and useful handbook describe the various forms in which preparations are obtainable, give prescriptions (again grouped according to systems), and list the most important maximum doses, and the most important drugs, with the preparations prepared from them, according to the *Pharmacopoea Helvetica*. Indexes are included of conditions for which drugs are indicated, and of the drugs themselves.

H. P.

Estudos cirúrgicos. 4a série

Eurico Branco Ribeiro. São Paulo, Livraria Atheneu José Bernades, 1945. 280 pages; illustrations. 24 x 16 cm.

Dr. Ribeiro is director of the Sanatorio São Lucas, and in this book he deals with a variety of surgical problems of which he has had practical experience, including plastic surgery, pyloric ulcer, ulcer of the anterior wall of the stomach, post-operative contingencies, etc. Illustrative case-histories of a number of patients treated at the Sanatorio São Lucas are given with descriptions of operative methods. The book contains photographic and diagrammatic illustrations.

Manual de alergia. Para el médico general

Milton B. Cohen. Versión directa del original inglés por el Dr. J. M. Cañadell. Barcelona, Ediciones Byp, 1947. 107 pages. 20 x 14 cm.

This is a translation from the original published in English in the USA and is addressed to general practitioners. The book includes a definition of allergy and chapters on its classification into different types, its clinical manifestations, diagnosis, treatment, some important allergens, allergic rhinitis, asthma, and serological reactions.

Chemotherapy yesterday, to-day, and to-morrow. The Linacre Lecture 1946

Alexander Fleming. Cambridge University Press, 1946. 39 pages; 7 illustrations. 18 x 13 cm. 2s. [£0.1]

In this lecture Sir Alexander Fleming reviews briefly the early work on chemotherapy of bacterial infections and the events leading to the discovery of the sulphonamides and of penicillin, and gives some description of the properties and production of these substances. After a lucid résumé of these "chemotherapeutic happenings" in which he himself has played so large a part, he describes briefly some of the other antibiotics recently introduced (gramicidin, tyrothricin and streptomycin), and indicates possible future developments. He concludes by an appeal for the foundation of a central institute for fundamental research in microbiology, which he describes as "the most important chemotherapeutic want in Britain at the moment." Such an institute would co-ordinate the work of investigators in many related fields and would provide facilities for research and development; had these been available in 1928, penicillin might not have had to wait 10 years. Should this appeal bear fruit, it would be a fine growth from the generous and far-sighted foundations of Linacre.

The Cambridge University Press publishes the lecture in this small paper-bound pamphlet with five clear diagrammatic illustrations (defaced, however, by one misprint in fig. 3) and two plates.

H. P.

The care of children from one to five

John Gibbens. Third edition. London, J. & A. Churchill Ltd., 1947. vii + 192 pages; 7 illustrations. 18 x 11 cm. 5s. [£0.25]

The care of children from one to five, by Dr. John Gibbens, is written in the same attractive conversational style as its predecessor, *The care of young babies*. The whole field of the development and care of the young child is covered in a most admirable way.

Unusual features are chapters dealing with such things as books and music, holidays, treats and picnics, the problem of sex and the care of young children in the tropics. Chapters have also been added on First Aid and the Care of the Sick Child.

This third edition, which has been almost entirely re-written, can be strongly recommended to mothers, nurses, and doctors in general practice.

Primeros cuidados a un accidentado

L. Gubern Salisechs. Barcelona, Ediciones Byp, 1946. 83 pages; 65 figures. 20 x 14 cm.

The first chapter of this book gives illustrative case-histories of injuries aggravated, in some instances fatally, by careless, inadequate or unskilled first-aid. The author goes on to indicate the correct first-aid treatment for various injuries and for shock, methods of artificial respiration and improvised transport for emergencies. He further gives useful information on what to avoid in applying first-aid treatment.

An approach to social medicine

John D. Kershaw. London, Baillière, Tindall and Cox, 1946. x + 329 pages. 22 x 14 cm. 15s. [£0.75]

The title of this book is to be taken literally. It is concerned with the development of a particular attitude towards medicine and towards society. While every good practitioner is actively concerned with the development of medicine in relation to social life, too few have accepted the challenge that medicine (among other agencies) must take an active part in influencing social activities in the interests of human well-being.

In order to make an appraisal of the disorders and disharmonies from which it suffers, Dr. Kershaw reviews the anatomy and physiology of society. He next discusses the developments of the major branches of medicine in relation to social activities. Finally, he considers some of the more urgent health-problems which society has created. Social medicine is a philosophy of health, and the last chapter appropriately deals with the human and social instruments of that philosophy.

In spite of its theoretical preoccupations this is a practical work, and is recommended not only to all medical men but also to those who claim to be intelligent, responsible citizens, for it is to this larger audience that the author makes his appeal. The succinct and necessarily dogmatic review of such a wide territory (with all its sins of commission and omission) satisfies a very real need of the average doctor, and the more enquiring are catered for in an excellent and ample bibliography.

R. Scott

L'année médicale pratique. 24e année

Edited by *Prof. Camille Lian.* Paris, Editions R. Lépine, 1945. xvii + 471 pages. 17 x 11 cm. Fr. 177

This annual is published under the general direction of Professor Camille Lian of the Hôpital Tenon, assisted by an editorial board of specialists in the various subjects covered. Its object is to extract the "marrow" from the medical literature of the past year and to present it in a condensed form for the benefit of medical practitioners who lack the time to assimilate the mass of published material, but who nevertheless need to know the important advances that have been made. The articles on each subject are written by specialists, who sift the material carefully, including only those points which are likely to be of real and practical importance to their readers, and present them in such a way that recourse to the original articles is unnecessary. While the emphasis is naturally placed on french work, important foreign contributions are noted as far as possible.

The main part of the journal consists of these articles arranged in alphabetical order, preceded by a classified list of titles. In addition there are: (*a*) a list of the most important new proprietary preparations of the past year, with in each case a brief description, and indications and directions for use; (*b*) an index of the principal manufacturers of proprietary drugs; (*c*) a list of the principal new apparatus and instruments; (*d*) a list of the chief medical books published during the year, under alphabetical subject-headings; and (*e*) an index to the articles in the main section.

A. H.-S.

Handbook of physiology and biochemistry

R. J. S. McDowall. Thirty-ninth edition. London, John Murray, 1946. xii + 898 pages; plates; 305 figures. 21 x 14 cm. £1 5s. [£1.25]

The first edition of this book appeared in 1848, its author was W. S. Kirkes of St. Bartholomew's Hospital, London, assisted by Mr. (afterwards Sir) James Paget, the lecturer in physiology at the hospital. The succeeding 8 editions were undertaken by different members of the hospital staff. In 1896 the 14th edition was undertaken by W. D. Halliburton of King's College, London, who brought out 17 editions in the next twenty-nine years. He was joined in 1928 by the present editor, and together they produced the 31st edition. Since 1930 R. J. S. McDowall alone has been responsible and has initiated 8 more editions.

The continued phenomenal success of this handbook cannot be attributed merely to tradition. In these days of expansion it is gratifying to notice that the present edition contains only 153 more pages than the original edition of 1848. A student's textbook should be a guide and not an encyclopaedia. In the reviewer's opinion, the author has quite correctly endeavoured to explain as simply as possible,

with the aid of some 300 illustrations, all that a student can be reasonably expected to know who studies physiology for five terms up to an ordinary degree standard. To avoid any misapprehension on this score, a test was made as follows. A recent 2nd M.B. physiology paper was chosen at random and the text relating to the specific material carefully read. There was no doubt in the reviewer's mind that from that standpoint the book was an unqualified success.

C. C. N. Vass

The science of seeing

Ida Mann & A. Pirie. Harmondsworth, Penguin Books (Pelican Books), 1946. 18 x 11 cm. 1s. [£0.05]

This is a competent presentation of several significant aspects of vision and its anomalies. Professor Ida Mann has contributed a series of delightful chapters dealing with the structure, development, and comparative anatomy of the eye, and on pathological disturbances. Miss Pirie has been responsible for the section with a biochemical bias, such as the excellent chapters on The Retina and Visual Purple, and on Cone Cells and Colour Vision, and that on Vision and Vitamins. The concluding chapters on Ocular Hygiene, the Blind Population and Ophthalmic Services complete an authoritative and balanced presentation.

L'œuvre des Pastoriens en Afrique Noire. Afrique Occidentale Française

Constant Mathis. Paris, Presses Universitaires de France, 1946. xi + 580 pages; illustrations. 22 x 14 cm.

The author's object in writing this interesting book is to give an account of the part played by Pasteur workers in combating some of the dread diseases of Africa. The period covered is from the year 1896, when the first Pasteur Institute in Africa was founded at St. Louis du Sénégal, to 1937 when the new Pasteur Institute was opened at Dakar. The book is in 7 parts, the first being a short historical sketch of the Pasteur Institutes in French West Africa. The 2nd and 3rd parts are devoted to an account of the directors who worked there throughout the period covered by the book, and to an account of Pasteur workers who have performed special missions in Africa. Part 4 deals with diseases prevalent in the country, and the measures taken to eliminate them or to reduce their toll of life. Part 5 gives an account of the Pasteur Institute at Kindia, its aims, organization and work. Parts 6 and 7 are devoted to the work of the Pasteur Institutes in Africa in the field of veterinary medicine. In conclusion the author sums up the immense benefit which the work of the Pasteur Institutes in Africa has been to the people of the country.

V. E. C. M.

Les contagions de la syphilis

G. Milian. Paris, Baillière et Fils, 1946. 205 pages; 28 figures. 24 x 16 cm.

This book, by a member of the Académie de Médecine, on the various ways in which syphilis is propagated, is based on wide clinical experience supported by an extensive study of the literature. The author quotes numerous illustrative cases, many of them having come under his own observation. The book is divided into four parts, of which the first occupies over half the book. The first chapter deals with the varying degrees of contagiousness at different stages of the disease. This is followed by a chapter covering modes of contagion and social sources, together with a note on the question of whether syphilis in the colonies was indigenous or imported by Europeans. The third chapter is a short one devoted to a description of *Treponema pallidum*, and is followed by a long chapter in which the author discusses fully the problems of reinfection and superinfection, or "supersyphilization". The first part of the book closes with a short chapter on syphilis in animals. The second and third parts are devoted to the various aspects of hereditary syphilis, and the fourth to the question of immunity: natural, acquired and experimental.

The book is illustrated with numerous photographs. There is no collected bibliography, but references are given in the text or as footnotes.

A. H.-S.

A practical handbook of psychiatry for students and nurses

Louis Minski. London, Wm. Heinemann (Medical Books) Ltd., 1946. 128 pages. 19 x 12 cm. 6s. [£0.3]

The author of this book has attempted an almost impossible task. In 16 chapters comprising only 120 pages he has tried to cover the vast range of modern psychiatry for the benefit of the medical student and the nurse. Special chapters, for instance, are given to occupational therapy and rehabilitation, the newer physical methods of treatment, psychotherapy and child psychiatry. Legal aspects of psychiatry, the psychoneuroses, nursing and general management, the etiology of mental disease and the various pyschiatric syndromes are all discussed. The chapters on physical treatments and occupational therapy and rehabilitation give a reasonable outline of these newer developments, but psychotherapy and child psychiatry are dealt with in chapters of only four pages each and are decidedly sketchy.

Readers of this book will get a bird's-eye view of the variety and scope of modern psychiatry. And if it does not satisfy fully the needs of either the nurse or the student, it may encourage those who read it to an increased interest in this rapidly-developing branch of medicine. Views expressed are definite and very much to the point. One or two statements of fact need correction, such as that pethidine has not the habit-forming characteristics of the opium alkaloids.

A textbook on the nursing and diseases of sick children for nurses by various authors

Edited by *Alan Moncrieff.* Fourth edition. London, H. K. Lewis & Co. Ltd., 1947. xiv + 744 pages; 144 illustrations. 22 x 14 cm. 30s. [£1.5]

At the end of this book the questions set at the final State examination for the supplementary part of the Register for Sick Children's Nurses for 1943 and 1944 are reproduced. These show the standard of knowledge required and the fourth edition of this well-known textbook does cover the ground required in a lucid and balanced manner. Professor Moncrieff has enlisted the aid of eleven contributors, all except two being members of the staff of The Hospital for Sick Children, Great Ormond Street. This book may, therefore, be said to reflect the teaching of that hospital.

In the nursing section, consideration is given to the care of the child in health as well as in disease, and orthopaedic surgery is described in detail. The second part of the book deals with diseases of children, and the various medical and surgical disorders and diseases are described in a comprehensive and orderly manner. The care and management of children in the tropics and their commoner diseases form the subject of the last chapter.

There is a most useful appendix dealing *inter alia* with pharmacology and therapeutics, nursing, recipes, physiotherapy, *x* rays, radium and medico-social work in a children's hospital.

The book can be confidently recommended to the nursing profession, not only for examination purposes, but also as a reliable and up-to-date text book on paediatrics.

J. M. S.

Medizinische Mikrobiologie. Parasiten, Bakterien, Immunität

Reiner Müller. Dritte, vermehrte Auflage. Berlin-München-Wien, Urban & Schwarzenberg, 1946. ix + 488 pages. 25 x 17 cm.

Austerity is the keynote of this work by Prof. Müller of Cologne. It contains very few illustrations, and these are only diagrammatic, and space is saved by including very little tabular matter, by the extensive use of small type, and by innumerable abbreviations. The book is divided into the three sections named in the title. The first is an independent whole, and entirely adequate, except that in the absence of any illustrations it must be very difficult for the student to form any clear ideas about such animal parasites as he cannot see for himself. The primary classification of bacteria in the second section is on a very simple morphological basis, separating them into only five groups: succeeding sections deal with viruses and fungi. The last-named section appears a better place for the *Actinomyces* than among the gram-positive bacilli, where they are actually described. The last section, on immunity, is more comprehensive than usual, and includes information about methods of immunization against particular infections which it is more usual to include with the description of the micro-organism concerned. There is much to be said for dealing with every aspect of each infection, including this one, in a single chapter, and making those on immunity more general and theoretical. The author has evidently been fortunate in obtaining access to the wartime literature of other countries, and much important recent work is mentioned. Sometimes it is no more than mentioned: for example, Lancefield's groups and Griffith's types of haemolytic streptococci are referred to, but with no hint of the practical uses of these classifications in epidemiological studies. The book contains a large amount of accurate information, but it is not in an easily-assimilable form.

The art of nursing

Florence Nightingale. Revised edition. Claud Morris Books Ltd., 1946. 52 pages; 1 plate. 18 x 12 cm. 6s. [£0.3]

Miss Nightingale's book *Notes on nursing*, written in 1859, has long been out of print and it is a pleasure to see it again, this time under a new title and with the text slightly expurgated.

The book is so full of deep understanding and shrewd commonsense that it is difficult to make selections for purposes of illustration. Her comments on the importance of accurate observation set a very high standard; she writes, "Is it not to be feared that observation as an essential part of medicine has been declining? 'There *must* have been *some* appearance had I but looked; let me try and remember what there was, that I may observe another time.' No, this is not what people say. They boldly assert that there was nothing to observe, not that their observation was at fault."

She understood occupational therapy eighty years ago. "Now you can have no idea of the relief manual labour is to you—of the degree to which the deprivation of manual employment increases the peculiar irritability from which the sick suffer. A little needlework, a little writing, a little cleaning would be the greatest relief the sick could have, if they could do it." Likewise, her stress on preventive work is apparent in every chapter.

Many readers will be surprised at the vigorous and witty style entirely free from Victorian sentiment.

On the subject of ventilation she writes "Windows are made to open; doors are made to shut—a truth which seems extremely difficult of apprehension." The publishers are to be congratulated on this attractive volume; the book is applicable to modern conditions because it deals with fundamental matters. It shows Miss Nightingale's amazing grasp of practical nursing detail combined with her outstanding administrative ability and political vision.

The birth of a child. Obstetric procedure in normal childbirth for those who attend women in labour

Grantly Dick Read. London, Wm. Heinemann (Medical Books) Ltd., 1947. viii + 99 pages. 18 x 12 cm. 5s. [£0.25]

The birth of a child by Grantly Dick Read is intended as an explanation, in simple non-technical language, of the author's methods for the relief of pain in childbirth by natural means. It consists, in the main, of a collection of papers published elsewhere with, in addition, the text of a lecture given to a medical society, some lecture notes, and personal accounts from patients who have found his methods successful. Inevitably there is a good deal of repetition, which is rather tiresome. The book, however, serves as a very useful introduction to the author's larger work, *Revelation of childbirth*. The lay reader, on the other hand, will find in its pages sufficient information for his purpose.

Surgical note-taking. A booklet for surgical dressers and clerks commencing clinical studies

Charles F. M. Saint. Fourth edition. London, H. K. Lewis & Co. Ltd., 1947. vii + 106 pages. 18 x 12 cm. 4s. 6d. [£0.225]

This little book has stood the test of time and has proved its worth to several generations of students. The average student takes very bad notes of his cases and should have such a book as this near at hand to help him in the difficult task of accurate observation. The illustrative cases serve as very good examples of note-taking and make the book more readable. Altogether a useful and practical book.

Z. C.

Eye surgery

H. B. Stallard. Bristol, John Wright & Sons Ltd., 1946. ix + 444 pages; 338 illustrations. 22 x 14 cm. £2 10s. [£2.5]

This work is a balanced survey of modern practice, even if it errs slightly in giving more on plastic surgery than most ophthalmic surgeons undertake. For the rest, the postgraduate student for whom the book is intended has clear and detailed instructions. Alternative methods are fully discussed, though the text is remarkably free from accounts of obsolete procedures. Since operating is an art—though an art based on science—the experienced surgeon can readily find passages in the text from which to dissent. More significantly, the book can be recommended as a straightforward account of "good, sound and honest practice"—to use a tribute that the author pays to his own teachers.

Meningitis meningocócica en la infancia: (meningitis cerebroespinal epidémica)

Walter Stirnimann. Traducción directa del alemán, notas y apéndice por el Dr. A. Ballabriga Aguado. Barcelona, Ediciones Byp, 1947. 112 pages. 20 x 14 cm.

This is a translation from German which deals with the epidemiology of meningitis; meningitic infections in infants, young children, and children of school age; sequelae; serous meningitis; and the therapeutics of meningitic infections. In the first chapter the author discusses the problem of infection, i.e. whether a predisposition of congenital origin may exist or whether some injury at birth or in the early days of a child's life may be a contributing factor. The author also discusses the difficulties of diagnosis in children at various ages, and symptoms and prognosis. He comments on the decline in mortality due to modern chemotherapy, and states that in recent cases he has seen no mental sequelae.

Spiders, ticks and mites: including the species harmful to man in Australia and New Guinea

F. H. Taylor & R. E. Murray. Sydney, School of Public Health and Tropical Medicine (University of Sydney), Commonwealth Department of Health, 1946. 275 pages; 185 illustrations. 24 x 14 cm.

The war in New Guinea brought many Australians into contact with diseases carried by insects, mites and ticks, and made them generally aware of the problems concerning dangerous arthropods. This book is intended to meet the interest which has been aroused, and to give information to those in isolated districts.

The first 234 pages deal with the systematics of the arachnids which may be harmful to man, and give data for the identification of the species. It is difficult to believe that this information will be of value to those who have not had a biological training, and without special experience, even a medical officer is unlikely to be able to make full use of keys or to be able to identify all the mites which are described. On the other hand, although little of the information is new, much of it is rather inaccessible, so scientific workers in New Guinea or northern Queensland should find this volume of considerable help, although there are many minor inaccuracies, especially in the section on Trombiculid mites.

The second section, of 38 pages, deals with the medical side of the problem. A third of the space is devoted to a useful account of the effects of bites of venomous spiders, with case-histories of a fair proportion of those which have occurred in Australia. A similar amount of space is given to tick paralysis. "Q" fever, which is believed to be carried by ticks, is not mentioned at all. Irritation caused by mites is described, and there is a full account of human scabies. Mite-borne typhus, though of so much importance in the war in the Pacific, is hardly mentioned at all.

Although it is claimed in the preface that "this book has been compiled so that it may be of service to the man on the land, the medical practitioner and the public in general," it was obviously planned and written during the war (the foreword is dated July 1945) and intended to be of use to military health authorities in the field. To be of more general use it requires replanning, particularly in the light of new information which was secret during the war and has now been released.

Kenneth Mellanby

Principles of the contact lens

H. Treissman & E. A. Plaice. London, Henry Kimpton, 1946. vii + 88 pages; 40 illustrations. 23 x 14 cm. 10s. 6d. [£0.525]

This book is designed to instruct the clinical ophthalmologist in the principles of the contact lens. A general description of contact lenses is followed by a brief optical revision and a discussion of the main indications for their use. The various types of lenses available are described and an account is given of the preliminary test which shows how contact lenses will help any particular case. The book ends with some discussion about tolerance, and the instruction of the patient in insertion and removal of the lenses. No details are given about the technique of the fitting or the manufacture of the lenses which are not the responsibility of the ophthalmologist. The book is well written and clearly illustrated, and fully achieves its stated purpose.

A. G. Cross

Elements of surgery

Fauset Welsh. London, Geoffrey Cumberlege, Oxford University Press, 1947. viii + 83 pages. 19 x 12 cm. 7s. 6d. [£0.375]

This book contains the substance of lectures given to nurses and will certainly be a useful help to first-aid workers and nurses. We hardly think that the author's hope that the book might also be useful to medical students is justified. The information given is accurate enough (though there are several minor inaccuracies), but it is fragmentary, ill-arranged, and does not give that sufficient emphasis on principles which is so essential for the medical student commencing the study of surgery. The author describes the chief characteristics of microbes without saying a word about antiseptics; and he gives an account of gangrene, haemorrhage and shock before dealing with the most important question of wounds. In the section dealing with the treatment of acute inflammation he mentions the giving of drugs by mouth or by injection "such as the sulpha drugs or penicillin" without giving any indication of the revolution in treatment brought about by the last-mentioned drug.

If this book is to be of real use to medical students it will need to be re-cast and enlarged. As an accompaniment to lectures to nurses it will no doubt prove very helpful. Several mistakes in spelling escaped correction.

Womanhood

Margaret Moore White. London, Cassell & Company Limited, 1947. 107 pages; 30 figures 22 x 14 cm. 7s. 6d. [£0.375]

Womanhood, by Margaret Moore White, is written in simple, clear language. It should prove useful to the engaged girl and newly-wed wife, as well as to the mother who wishes to explain to her growing daughter certain of the developing processes in her body.

As the space available for dealing with Bottle-feeding and the Problems of Infancy and Early Childhood is necessarily very limited, it might have been well to have made only a passing reference to the first and to have omitted the second. There are many excellent books now available dealing with all aspects of infant-care.

On the whole this is an excellent book and could be recommended, although one or two opinions are expressed from which the lay reader's own medical adviser may differ.

X-rays

B. L. Worsnop & F. C. Chalklin. Second edition. London, Methuen & Co. Ltd., 1946. vii + 126 pages; 47 illustrations. 17 x 11 cm. 5s. [£0.25]

In the preparation of the second edition of his monograph on *x* rays, Dr. Worsnop has enlisted the help of Dr. Chalklin. Together they have succeeded in producing a clear, compact work on the physics of *x* rays. It should prove both of value and interest to the two classes of medical readers most concerned, namely the practising radiologist and the radiological student. The former will be shown what is new and reminded of much that he has forgotten; whilst the latter will be provided with a readable, straightforward and simple account of a subject usually considered tedious by doctors.

M. Lederman

The human approach. A book for medical students

Henry Yellowlees. London, J. & A. Churchill Ltd., 1946. vii + 189 pages. 21 x 14 cm. 10s. 6d. [£0.525]

Designed as an introduction to psychological medicine, this book never loses sight of the fundamental doctor-patient relationship and would be sound preliminary reading for any students preparing for work involving human relationships. It is addressed to medical students just entering the clinical period of their training, in which is introduced "an entirely new factor—namely, human nature." Clinical material, the author points out, unlike that in the dissecting room, may lie, sulk, deceive, and announce its opinion of the student.

Dr. Yellowlees, from his large experience of psychiatry and of teaching medical students, describes in straightforward language the psychological mechanisms involved in the problems which face every young doctor. His book is calculated both to arouse interest in specialized medical psychology and to be of fundamental use to all engaged in any form of medicine. It is based on the conception of psychosomatic unity, and reiterates the presence of both psychological and physical factors in all disease and the consequent need for every medical man to have a working knowledge of medical psychology.

Included is a section on Doctor and Lawyer, giving useful information often gained only by the hard way of experience. This is followed by a chapter entitled Psychiatric Oddities, which describes some of the unusually difficult people, both patients and their relatives, with whom the student may have to deal, illustrated by amusing anecdotes from the author's own experience. Under The Word "GO" Dr. Yellowlees attempts to reply to the fundamental enquiries of students at the beginning of their course. He suggests that the ideals demanded in the service of science are: humility, intellectual honesty, courage, the enquiring mind—and, added to these, the capacity for wonder. An appendix on sane psychology gives a survey of the situation which prompted the author to write this most readable and stimulating book.

H. P.

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Books Received

May 1947—September 1947

Many of the books listed will be, or have already been, reviewed in the Bulletin.

Air Ministry. *Handbook of preventive medicine.* (Air publication 1269B.) 1947. His Majesty's Stationery Office, 7s. 6d. [£0.375]

Anderson, J. R. *Ocular vertical deviations.* British Journal of Ophthalmology, Monograph Supplement XII. 1947.

Bariéty, M. & Brocard, H. *Les septicémies à staphylocoques.* 1945. Baillière (Paris).

Barraud, A., Nager, F. R., Rüedi, L., Schlittler, E. & Taillens, J.-P., editors. *Lehrbuch der Hals- Nasen- Ohren- und Mundkrankheiten.* 1947. S. Karger (Basel), sw. fr. 60

Beaumont, G. E. & Dodds, E. C. *Recent advances in medicine.* 12th ed. 1947. Churchill, £1 1s. [£1.05]

Binger, C. *The doctor's job.* 1946. Allen & Unwin, 12s. 6d. [£0.625]

Board of Control (England and Wales). *Prefrontal leucotomy in a thousand cases.* 1947. His Majesty's Stationery Office, 6d. [£0.025]

Brain, W. R. *Diseases of the nervous system.* 3rd ed. 1947. Geoffrey Cumberlege, Oxford University Press, £1 17s. 6d. [£1.875]

British Journal of Surgery. *Wounds of the head.* (War Surgery Supplement No. 1.) 1947. Wright, £1 10s. [£1.5] (Free to subscribers)

British Red Cross Society. *Report for the year 1946.* [1947.] British Red Cross Society

Brunschwig, A. *Radical surgery in advanced abdominal cancer.* 1947. University of Chicago Press, £2 2s. [£2.1]

Burn, J. L. *Recent advances in public health.* 1947. Churchill, £1 5s. [£1.25]

Cameron, A. T. *Recent advances in endocrinology.* 6th ed. 1947. Churchill, £1 1s. [£1.05]

Chailley-Bert, P. *et al. Aptitude aux sports et contrôle médical.* 2e éd. 1943. Baillière (Paris)

Clark-Kennedy, A. E. *Medicine. Vol. I. The patient and his disease.* 1947. Livingstone, £1

Clay, H. H. *The sanitary inspector's handbook.* 5th ed. 1942. Lewis, 18s. [£0.9]

Cochrane, R. G. *A practical textbook of leprosy.* 1947. Geoffrey Cumberlege, Oxford University Press, £2 2s. [£2.1]

Collis, E. *A way of life for the handicapped child. A new approach to cerebral palsy.* 1947. Faber, 10s. 6d. [£0.525]

Colson, J. H. C. *The rehabilitation of the injured. Vol. 2. Remedial gymnastics.* 1947. Cassell, £1 10s. [£1.5]

Comerford, J. *Health of the unknown. The story of the Peckham experiment.* 1947. Hamish Hamilton, 7s. 6d. [£0.375]

Crawford, A. M. *Materia medica for nurses.* 6th ed. 1947. Lewis, 5s. 6d. [£0.275]

Cyriax, J. *Rheumatism and soft tissue injuries.* 1947. Hamish Hamilton, £2 2s. [£2.1]

Davidson, L. S. P. & Anderson, I. A. *A textbook of dietetics.* 2nd ed. 1947. Hamish Hamilton, £1 1s. [£1.05]

Dawes, B. *Man and animals, what they eat and why. A manual of nutrition.* 1947. Longmans Green, 7s. 6d. [£0.375]

Department of Scientific and Industrial Research. *Report of the Water Pollution Research Board: with the report of the Director of Water Pollution Research, 1st July 1939 to 31st December 1945.* 1947. His Majesty's Stationery Office, 1s. 3d. [£0.063]

Dewberry, E. B. *Food poisoning: its nature, history and causation, measures for its prevention and control.* 2nd ed. 1947. Leonard Hill, 17s. 6d. [£0.875]

Durán Arrom, D. De G. *Propedeutica de patologia circulatoria en las profesiones.* 1947. Ediciones Morata (Madrid), ptas 40

Duthie, E. S. *Molecules against microbes.* (Introduction to Science No. 6.) 1946. Sigma, 6s. [£0.3]

Edge, P. G. *Vital statistics and public health work in the tropics including supplement on the genealogy of vital statistics.* 1947. Baillière, 15s. [£0.75]

Egypt. Ministère de l'Hygiène Publique. *La semaine de l'Egypte pour la lutte contre le cancer, 23-30 Novembre 1938.* 1941. Schindler (Cairo)

Ewart, E. D. *A guide to anatomy: for students of physiotherapy and electrotherapy.* 6th ed. 1947. Lewis, £1 5s. [£1.25]

Ewing, I. R. & Ewing, W. G. *Opportunity and the deaf child.* 1947. University of London Press, 9s. 6d. [£0.475]

Franco, B. B. *Información sobre la lucha antituberculosa en España y memoria correspondiente al año 1944.* 1945. Publicaciones del Patronato Nacional Antituberculoso (Madrid)

Frantz, V. K. & Harvey, H. D. *Introduction to Surgery.* 1946. Oxford University Press (New York), £1 5s. [£1.25]

Fraser, R. *et al. The incidence of neurosis among factory workers.* (Medical Research Council. Industrial Health Research Board Report No. 90.) 1947. His Majesty's Stationery Office, 1s. 3d. [£0.063]

Frazer, W. M. *Duncan of Liverpool: being an account of the work of Dr. W. H. Duncan, Medical Officer of Health of Liverpool 1847-63.* 1947. Hamish Hamilton, 8s. 6d. [£0.425]

Gesell, A. & Amatruda, C. S. *The embryology of behavior.* [1947.] Hamish Hamilton, £1 1s. [£1.05]

Gill, G. H. *Dust and its effects on the respiratory system.* 1947. Lewis, 5s. [£0.25]

Gräub, E. *Tuberkulöse Reinfektion beim Rinde.* 1947. S. Karger (Basel)

Groves, E. W. H. *Synopsis of surgery.* Edited by C. P. G. Wakeley. 13th ed. 1947. Wright, £1 5s. [£1.25]

Grüneberg, H. *Animal genetics and medicine.* 1947. Hamish Hamilton, £1 1s. [£1.05]

Guggisberg, H., editor. *Lehrbuch der Gynäkologie.* 2. Aufl. 1947. S. Karger (Basel)

Harvey, W. C. & Hill, H. *Insect pests.* 2nd ed. 1947. H. K. Lewis, 14s. [£0.7]

Heimann, H. L. & Wilson, D. *Nurses' pharmacopoeia and pocket book of useful ward information.* 5th ed. 1946. Baillière, 4s. [£0.2]

Hentschel, C. C. & Cook, W. R. I. *Biology for medical students.* 4th ed. 1947. Longmans Green, £1 5s. [£1.25]

Hern, K. M. *Physical treatment of injuries of the brain and allied nervous disorders.* 1947. Baillière, 10s. 6d. [£0.525]

Hill, H. *Pasteurisation.* 2nd ed. 1947. Lewis, £1 1s. [£1.05]

Hill, H. & Dodsworth, E. *Food inspection notes.* 2nd ed. 1947. Lewis, 6s. [£0.3]

Houghton, M. *Aids to practical nursing.* 5th ed. 1947. Baillière, 5s. [£0.25]

Illingworth, C. F. W., editor. *Textbook of surgical treatment including operative surgery.* 3rd ed. 1947. Livingstone, £1 12s. 6d. [£1.625]

Jellinek, S. *Dying, apparent-death and resuscitation.* 1947. Baillière, 10s. 6d. [£0.525]

Jones, W. H. S. *The medical writings of Anonymus Londinensis.* 1947. Cambridge University Press, 12s. 6d. [£0.625]

Jorpes, J. E. *Heparin in the treatment of thrombosis. An account of its chemistry, physiology and application in medicine.* 2nd ed. 1946. Geoffrey Cumberlege, Oxford University Press, 18s. [£0.9]

Klueva, N. G. & Roskin, G. I. *Bioterapiya zlokachestvennikh opookholay.* 1946. Akademiya Meditsinskii Nauk SSSR (Moskva)

Kolff, W. J. *New ways of treating uraemia. The artificial kidney, peritoneal lavage, intestinal lavage.* 1947. Churchill, 10s. 6d. [£0.525]

Le Maistre, E. H. *Physical education.* 1945. Oxford University Press (Melbourne), 11s. 6d. [£0.575]

Lewis, H. K. & Co. Ltd. *Supplement to the catalogue of Lewis's medical, scientific and technical lending library: including a classified index of subjects with the names of those authors who have treated upon them. Supplement, 1944-1946.* 1947. Lewis, 5s. [£0.25] (To subscribers to the library, 2s. 6d.)

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Introduction

There has recently been published an account of the six public lectures delivered to the XI International Congress of Pure and Applied Chemistry which was held in London last year. From this account it is seen that four of the six lectures were clearly of biochemical substance, while the fifth, that delivered to the section of Organic Chemistry, was largely devoted to natural materials of the liveliest concern to biochemists. Since the Congress was concerned with chemistry in the widest sense of the word, the devotion of such a large proportion of interest to matters of biological import once again emphasizes the immense influence which biochemistry is exerting upon the primary sciences.

It is good that the emphasis on the " chemistry " in " biochemistry " should be sounded, but such an emphasis carries with it two potential dangers. First, the attractiveness of those investigations which are devoted to the chemistry of substances of biological significance may detract seriously from the fundamental work on chemistry for its own sake, work upon which future developments inevitably rest. For example, progress in the development of methods for the synthesis of penicillin are impeded by the paucity of fundamental knowledge concerning the chemistry of four-membered rings containing a nitrogen atom. It is of the greatest importance to biochemistry and to medicine that chemists should never cease to explore the

reactions and properties of purely synthetic substances, even though such substances have apparently no connexion with biology or with medicine.

The second danger is more subtle but nevertheless just as real. It is of the highest importance that the spectacular results which have already been achieved by a purely chemical attack upon biological materials should not divert the attention of biochemists from the core of the problem of biochemistry—the study of the enzyme system within the cell. Although chemistry and biochemistry must necessarily overlap to a substantial extent, the chemist is primarily interested in the fragmentation and synthesis of molecules in the laboratory, while the biochemist should be, and is, more fundamentally concerned with the changes which substances undergo within a living system, both in the building up of such a system, and in the maintenance of it by metabolic processes.

In this country the dynamic approach to biochemical problems was largely founded by the investigations and ideas of the late Sir Frederick Gowland Hopkins, whose famous dictum, " Life is the expression of a particular dynamic equilibrium which obtains in a polyphasic system ", is quoted in the article, Biochemical Integration in Cellular Function, by Dr. Ernest Baldwin, a pupil of Gowland Hopkins, which appears in the present issue. It is therefore not inappropriate that this issue of the *British Medical Bulletin* should be regarded as a tribute to the work and memory of Sir Frederick Gowland Hopkins. The article on Gowland Hopkins by Joseph and Dorothy Needham has been written from a personal point of view which, it may be hoped, will assist many who did not know Hopkins to appreciate something of the charm and inspiration which he shed upon those around him. It is fitting, too, that the ideas and teaching of Hopkins and his school should recently have been ably summarized in a textbook by Ernest Baldwin entitled *Dynamic aspects of biochemistry* (Cambridge University Press, 1947), a book which will almost certainly inspire the teaching of the subject for many years to come.

It is one of the triumphs of biochemistry that it provides a potent integrating force in medicine which, until the present time, had been completely lacking. For instance, the integration of such diverse branches of medicine as bacteriology and nutrition on a biochemical basis is now so widely accepted that the articles on Metabolic Processes in Micro-Organisms by Drs. Marjory Stephenson & Ernest Frederick Gale, and Wider Aspects of Studies of the Nutrition of Micro-Organisms by Dr. D. D. Woods naturally fall within their places in the present volume. Again, The Development of British Anti-Lewisite (BAL) by Prof. Peters and his colleagues at Oxford provides an excellent example of the value of the biochemical approach to an apparently complex pathological problem, with the enzyme system as the focus of attack. Findings of the greatest theoretical and practical significance, which are ably discussed by Prof. Peters, have accrued from this work, while his collaborator, Prof. R. H. S. Thompson, deals with the Therapeutic Applications of British Anti-Lewisite which have subsequently been developed upon general lines. The fact that biochemistry can provide a rational treatment for the toxic conditions due to arsenic, gold and other metals, is but one of the many vindications of the theoretical approach followed by Peters and his school.

The work of Beadle, Tatum and others, on the nutritional requirements of *x*-ray-induced mutants of *Neurospora crassa* and other organisms, has provided a previously unexpected line of attack upon the problems of the biochemistry of intermediary metabolism, but the implications of this work are very wide, and are only now being realized. Their application to human genetics is still to be developed, but in his article on Human Biochemical Genetics, Mr. Tracey recalls the pioneer work of Garrod and others upon inborn errors of metabolism, the study of which has received a new impetus from the recent experimental investigations on micro-organisms.

The article by Mr. N. W. Pirie entitled Development of Ideas on the Nature of Viruses deals in a critical manner with some of the speculative ideas which have abounded since the pioneer work of Stanley and his colleagues on the so-called crystallization of plant viruses. But such criticisms need not detract from the significance of the results of this purely biochemical attack upon a problem which was originally one confined to pathologists or bacteriologists. The problems of immunology have provided the material for the irruption of biochemistry into another field not previously

explored from such an angle, and this aspect of the work is ably discussed by Prof. A. Wormall in his article Contributions of Chemistry to the Problems of Immunology. The articles on Fibrous Proteins as Components of Biological Systems and on Some Newer Knowledge of Plasma Proteins, by Dr. Kenneth Bailey and Dr. R. A. Kekwick respectively, describe work which is mainly directed towards the problem of the identity and nature of the building-stones of biological systems, while Amino-Acids in Nutrition by Dr. A. Neuberger brings us back once more to the dynamic aspects of biological equilibria.

The articles in the present number of the *British Medical Bulletin* illustrate the significance of the progress in medical science towards the study of smaller and smaller units. In the early days the organ was the element for study, but the work of Bichat on the fundamental concept of tissues and later the investigations of Virchow elaborated the idea of the cell as the essential unit in all tissues and organs. Modern biochemistry has developed this idea still further, and now regards the underlying fundamental unit as the molecule. It is from this idea that the unifying influence of biochemistry upon the diverse phenomena of biology and medicine springs. Whatever their origin, cells are found to have certain elements of structure in common. They all contain proteins, fats and carbohydrates. Their metabolic processes are catalyzed by enzymes which are surprisingly similar in nature and function wherever they may be found throughout the species. Enzymes co-operate with co-enzymes, which again are widespread to a surprising degree. Co-enzymes in many instances are constructed from essential constituents of the food, hitherto known as vitamins when human or animal nutrition is under consideration. That many micro-organisms nutritionally depend upon a supply of such vitamins has been a discovery of great practical and theoretical significance.

By thus revealing a common ground-plan among so many different biological systems, the biochemist has provided an understanding to the solution of many medical problems, the approach to which could previously be only empirical. To such developments the biologist and the medical man, no less than the biochemist, owe an immense debt to the intuitive insight of Frederick Gowland Hopkins.

F. G. Young

THE EDITOR wishes to acknowledge the valuable help given by Professor F. G. Young of the Department of Biochemistry, University College, London, in the planning of the Symposium of this number and for writing the Introduction.

* * *

We would also like to draw the attention of our readers, especially of those abroad, to the article by Dr. F. H. K. Green which appears at the beginning of Part II of this number (page 352), on the origin, constitution and functions of the Medical Research Council. During the war Dr. Green was secretary of the MRC War Wounds Committee and of the Therapeutic Trials Committee and is now Assistant Secretary to the Council. This authoritative article, with its useful table showing the principal research establishments of the MRC, should prove of great value to those interested in medical research in Great Britain.

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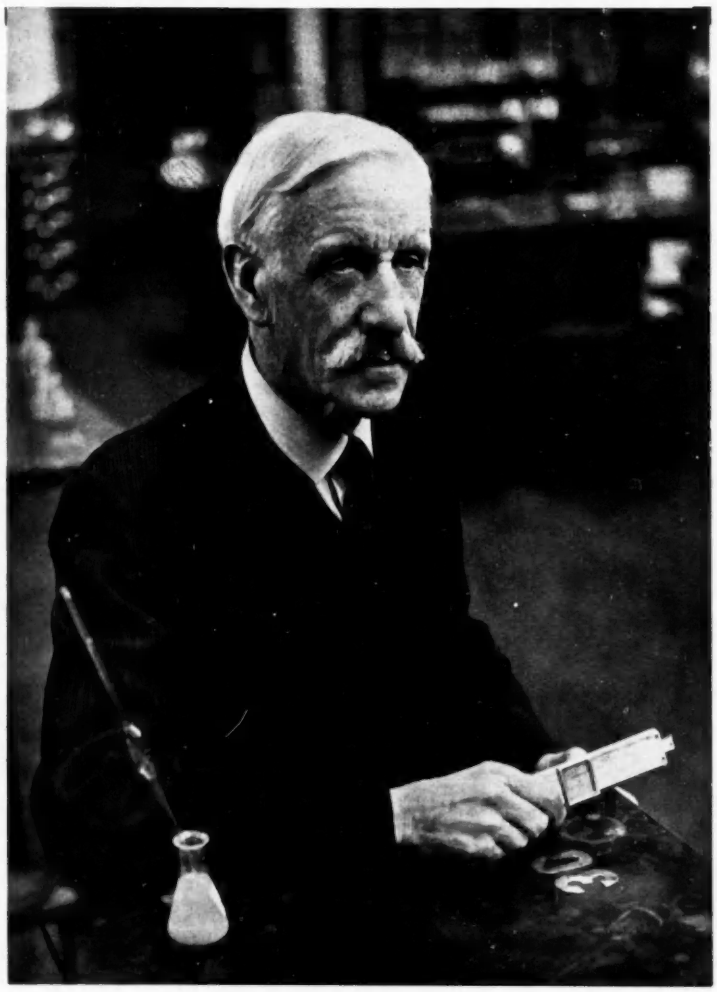

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SIR F. GOWLAND HOPKINS

1861–1947

SIR FREDERICK GOWLAND HOPKINS
O.M. P.R.S.

JOSEPH AND DOROTHY NEEDHAM

In writing something on "Hoppy" (as he was universally known in the world of biochemists) by way of introduction to this special number of the *British Medical Bulletin*, it will be our aim to try to give some impression, however faint, of his personality, supplementing the accounts of his life and work which have already appeared.[1] Our excuse may be that for more than twenty-five years he stood *in loco parentis* to us, as to all other Cambridge biochemists of our generation.

It is therefore not necessary to repeat in great detail the story of his life and principal investigations—his early work in a toxicological laboratory, his medical training at Guy's Hospital, his invitation to Cambridge in 1898 by Sir Michael Foster, the tutorship at Emmanuel, the praelectorship at Trinity, a chair in 1914, a great new building in 1925, the Order of Merit, the Nobel Prize, and so on. Widely known, too, is the course of his researches; first on gout and uric acid and the pigments of butterflies, then on amino-acids with the discovery of tryptophan (with Cole), then on the accessory food-factors now called vitamins, next to muscle-contraction and lactic acid (with Fletcher); and finally to oxydo-reductions and the discovery of glutathione—a subject which kept his interest during most of the period between the two World Wars—until at the end he returned with more precise analysis to his earliest interest, the pterine pigments of lepidoptera, now with much wider physiological significance.

The first twenty years of Hopkins' work and teaching were carried out in an extremely old and uncomfortable building in Corn Exchange Street, many of the rooms of which were semi-cellars. We can well remember this, as it lasted in partial use until the construction of the present Institute in Tennis Court Road in 1924. Much of the equipment was antique, too; for example, a centrifuge which was mounted on boards and had no arrangements for securing it to a base, used to ride all over the floor of a cellar when in operation. It was in these rooms that the rat-colony was kept; its entire feeding and upkeep during the classical investigations on vitamins in 1910 were done by Hopkins himself. Upstairs was the shelf on which had stood in the sunlight the bottle of acetic acid which had led to the discovery of the glyoxylic test for tryptophan. Below were the ancient benches on which "Charles" had cut up the quarters of horses towards the end of World War I for the extraction of glutathione.

The year 1920 saw expansion into a building hardly less queer than that in Corn Exchange Street, namely an old chapel in Downing Place where the space level with the galleries had been specially floored. A bridge connected the main part with an annexe in which Hopkins himself worked. Here developed all the lines of research which were afterwards to characterize Hopkins' institute—intermediary metabolism, especially that of sulphur compounds; bacterial metabolism; the chemistry of muscular contraction; the precise physico-chemical study of enzymes and pigments; and embryological and zoological biochemistry.

By no means the least important of the rooms in this building was the library (Hopkins was always ready to die in the last ditch for the departmental-library principle) and tea-room. Throughout the fifty years of Hopkins' work at Cambridge there were held weekly or fortnightly tea-club meetings, at which one or other of the research-workers would give an account of work in progress or nearing completion. The standard of criticism at these meetings was extremely severe, so that the speaker met with more rational and constructive comment there than he was ever likely to encounter at subsequent meetings of public societies to which he might communicate his work. It was at these meetings that Hopkins' genius particularly showed itself; he invariably made every paper seem interesting, what the author might have dully presented he illuminated with a flow of historical allusions and valuable suggestions springing from his profound intuitive insight into the structure and functions of the living cell. No one could speak or act as if blinded by passion or prejudice when in the presence of a leader so objective yet so encouraging, so affectionate yet so penetratingly quizzical, whose insight was conveyed by hints and odd remarks to which no one could object, but which one disregarded at one's peril.

Perhaps these meetings were so searchingly critical precisely because of "Hoppy's" own extraordinary charm and kindness. Under his aegis almost anything could be said without fear of offence. This was, in fact, his most outstanding personal quality; he was a living embodiment of the Confucian maxim that one should behave to everybody as one receiving a great guest. The humblest laboratory assistant or the youngest research worker was always sure of a welcome, and a hearing, unhurried and attentive, much longer than he was likely to get from any other scientific man of the same standing or generation. Hopkins had faith in people. Colleagues were known to remark lightly that "All Hoppy's geese are swans", but they forgot that there is an induction process by which certain geese may be turned into swans if given the hormone of encouragement.

It was undoubtedly for these reasons that when we attempted recently to recapture some characteristic sayings of Hopkins, some "famous remarks" of Johnsonian flavour, we found it quite impossible to do so. This fact is of interest in itself. He was too courteous, in a way too self-effacing, to allow himself to be the author of epigrams which might hurt anyone; he expressed himself so diffidently, and above all he spent so much of his time listening to other people, that his essence cannot be treasured in a few *bons mots*. He was a great giver and receiver of moral support—if he gave freely of it to all his collaborators and colleagues, he also needed it, for he frequently passed through periods of depression. And this was one of his

[1] E.g.—*Brit. med. J.* 1947, 1, 742
Lancet, 1947, 1, 728
Nature, Lond. 1947, 160, 44

secrets, that he was open to receive it from the most junior of his research workers, so that they did not feel he was encouraging them like some *deus ex machina*, but as one of themselves; in other words he fully understood and practised the great doctrine of leadership *from within* and not from above.

Anyone who obtained the impression from what has been said that Hopkins had a colourless personality would indeed be wide of the mark. He did not say things that make the stuff of anecdotes, he did not speak much on the radio or appear prominently in the public press, he did not engage in polemics. But he had the knack of surrounding himself with people of striking personality, such as A. Szent-Györgyi (the hungarian Nobel Prizewinner and discoverer of the chemical constitution of vitamin C), J. B. S. Haldane (afterwards Professor of Genetics at London), Marjory Stephenson (one of the first women to become F.R.S.), T. S. Hele (later Master of Emmanuel and Vice-Chancellor of the University), etc., etc. But nothing ever put "Hoppy" in the shade. No one could fail to recognize in the little figure, rubbing its eyes in a characteristic gesture during a conference, loitering with overcoat unbuttoned in the hall, or proceeding with ruminative walk past the colleges, the authentic gold of intellectual inspiration, the *Fundator et Primus Abbas* of biochemistry in England.

The pattern completes itself when we look at the various practices which he established. Contrary to what has been known in some english and many continental laboratories, Hopkins would never put his name to any scientific paper for which he had not himself done a considerable part of the manual and experimental work involved. Although no doubt great results are to be achieved by the direction of large teams, he was never interested in forcing the diverse talents of his younger colleagues into the funnel of one problem, as he could well have done in such matters as vitamins or oxydo-reductions. On the contrary, he was always looking out for originality, and encouraged the smallest sprouts of it to develop in their own way. Sometimes a young worker would devote himself to some subject which "the Professor" had initiated and then dropped, and make a life-work of it—this happened with vitamins, with muscle-biochemistry, and with oxidation-reduction enzymes. In other cases, a young worker would start something new with every possible encouragement from Hopkins—this happened with the metabolic chemistry of micro-organisms, with embryological biochemistry, and with the study of plant-pigments. One of us certainly will never forget how quickly Hopkins appreciated the fascination of the hen's egg as a closed-box system of chemical transformations; he said that there were many lifetimes of work in it, and it put him in mind of a discussion he had had at Michael Foster's breakfast-table some twenty years earlier.

If, then, Hopkins' outstanding personal characteristic was a universal courtesy, even a capacity to suffer fools gladly (knowing that some fools may change into wise men in the process), what was his outstanding intellectual characteristic? Originally, we believe, it was a deep intuitive faith in the explicability of the biochemistry of the living cell—the same faith which once inspired Aristotle when, in the face of the apparently infinite complexity of living forms, he nevertheless maintained that it was possible to classify them, and proceeded to do so in at least a preliminary way. Having in mind what we know now about the numbers of species of arthropods, and how little we yet know about the physiology of invertebrates in general, Aristotle's faith seems indeed extraordinary. Hopkins was of the same lineage, for at a time when it could be said, or had until shortly before been currently said, "Tierchemie ist nur Schmierchemie", he knew better. He was not only an organic chemist who could isolate substances from living tissues and study their chemical structure; he was a *bio*chemist who could in imagination perform the synthetic process of building back the living cell and of visualizing what processes were going on in it. And this was all the more extraordinary in that he was himself not the direct pupil of any of the pioneers of biochemistry. Here came into play his intuition. At a relatively late period one of the more provocative of the younger research workers opined that "Hoppy" was not a great experimentalist, and on being asked why, replied that it was because he did not need to do experiments, he knew which way the cat would jump beforehand, and only needed to carry out practical work to demonstrate what his insight had already told him was true. This was not at all an unfair judgement, though paradoxical in that Hopkins was in fact a brilliant practical chemical manipulator and experimentalist; a most accomplished laboratory worker. By 1914 Hopkins had transmuted the old german jibe into the famous definition: "Life is a dynamic equilibrium in a polyphasic system."

As to scientific literature, Hopkins was by no means a despiser of it, as some eminent experimentalists have been, trusting in their own originality and in the mistakes of others. He read a great deal, and often inspired his listeners with enthusiasm for neglected pioneers such as Thudichum, the investigator of the brain lipids; or de Rey Pailhade, the discoverer of "philothione", the hypothetical substance which preceded the real glutathione. In later stages, the walls of the laboratory were decorated with engravings of Lavoisier, Harvey, Boyle, Hales, Scheele, etc., together with an original manuscript of Liebig. Hopkins' lectures to the advanced class were often largely historical. One characteristic which all his pupils remember was his trick of waving about in a beaker of water the feather of a tropical bird, from which the water-soluble pigment turacin comes out—anyone who was not interested in such a phenomenon would, he used to say, never make a biochemist. It was equally characteristic of him that when, on one occasion, one of the more phlegmatic young research-workers was not perceptibly excited by it, he remarked that of course one must in this test make allowances for temperament. At the very close of his life, when he was perhaps remembering more of his youth, he told another pterine investigator that as a boy he had taken the wings of a butterfly and heated them in a spoon on the kitchen range of his home; when the pigments dissolved in the water he was extremely astonished and delighted.

So far as we can remember Hopkins had no particular hobby except reading, which he did largely in a fairly unselective way, on all kinds of subjects, such as history, archaeology and the like. One of his daughters was destined to become a distinguished archaeologist, doubtless not without some encouragement from these broad interests of her father's. Though he never visited any of the remoter parts of the world, he always took a great interest in people

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BIOCHEMICAL INTEGRATION IN CELLULAR FUNCTION

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1 Intracellular dynamics
2 Source of muscular energy
a Phosphorylation
b Glycolysis
c Oxidation
3 Extramuscular energy

"La vie," declared Lavoisier in 1780, "est une fonction chimique". Liebig, echoing Lavoisier's belief, in an address to the Chemical Section of the British Association in 1837, expressed his conviction that in the newly-founded science of organic chemistry, biology could find its most powerful ally. But the cry of the chemists that "Tierchemie ist Schmierchemie", and the obscurantist tactics of many biologists, delayed the large-scale application of chemical methods to biological problems for more than 50 years. A few, notably Voit and his pupil Rubner, followed in Liebig's footsteps and, in 1894, Rubner could announce his calorimetric demonstration that the amount of energy expended by a living organism is exactly equivalent to the energy set free by metabolism within the body; that living, like non-living systems, conform to the principle of the conservation of energy.

1. Intracellular Dynamics

For the early development of its dynamic side, biochemistry owes its greatest debt to Gowland Hopkins, whose recent death has deprived us of the subject's most powerful protagonist and its most inspired and inspiring leader. Of his many speeches and addresses perhaps none was more significant or far-sighted than that delivered to the Physiological Section of the British Association in 1913. Setting aside the "vital forces" as an unnecessary postulate, he pointed out with incisive clarity the greatness of the part the organic chemist could play in the development of biochemistry. "One reason", he said,

> which has led the organic chemist to avert his mind from the problems of Biochemistry is an obsession that the really significant happenings in the animal body are concerned in the main with substances of such high molecular weight and consequent vagueness of molecular structure as to make their reactions impossible of study by his available and accurate methods . . . So far from this being the case, recent progress points in the clearest way to the fact that the molecules with which a most important and significant part of the chemical dynamics is concerned are of a comparatively simple character.

Later in the same address came what is perhaps Hopkins' most celebrated utterance:

> On ultimate analysis, we can hardly speak at all of living matter in the cell; or at any rate we cannot, without gross misuse of terms, speak of the cell life as being associated with any one particular type of molecule. Its life is the expression of a particular dynamic equilibrium which obtains in a polyphasic system . . . but "life", as we instinctively define it, is a property of the cell as a whole, because it depends upon the organisation of processes, upon the equilibrium displayed by the totality of the co-existing phases.

FREDERICK GOWLAND HOPKINS

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who came from them and welcomed them to his laboratory, which thus acquired and maintained throughout a thoroughly international character. Before the first World War he had a number of japanese pupils, but later only one—an odd character who caused some confusion in the laboratory by coming in late at night to work (it was typical of the institute that it was always available for work all night) and hanging his coat and hat on the thermostat-rod of an incubator. China and India were represented and North and South America very much so, while all the countries of Europe and the Near East contributed at one time or another their quota of investigators, as did all the Dominions of the British Commonwealth. Frequently a postcard would arrive filled with signatures from bodies such as the "Hoppy Club of San Francisco". Correspondingly, the presentation volume *Perspectives in biochemistry* which he received upon the occasion of his 75th birthday, was a success altogether unexpected by its publishers, the Cambridge University Press, and went into three editions.

From what has already been said, it will be obvious that Hopkins was naturally a democrat. We shall always remember a meeting, held in 1942, which was designed to inform all those working in the institute, including especially the laboratory assistants and cleaners, in semi-popular language, of what exactly were the various pieces of war research being carried out in the institute. Each speaker was given only three minutes. It was expected and understood that the Professor, in view of his age and eminence, would take longer; but no, the Nobel Prizewinner and ex-President of the Royal Society said his say in exactly the same time as all the others. The meeting achieved its purpose of intensifying the war effort of the institute.

A perfectly sympathetic personality is not usually achieved without cost. There is no doubt that Hopkins had a very severe struggle in his early years, and at the end of his Emmanuel tutorship he was so overworked that he suffered a kind of nervous breakdown for a short time. Daily, hourly, as everyone must with something new to give to the world, he battled with the philistines. Unfortunately, in his very last years he also had much to suffer, when increasing physical disabilities coexisted with undiminished retention of intellectual power and curiosity. But it all resulted in a personality which drew from his colleagues not only intellectual admiration but deep affection and even veneration. So many of the Taoist paradoxes were found to be applicable to Hopkins—"The Sage follows after things, in order that he may control them"—"The Sage has no personal wishes, therefore all his desires are fulfilled". Inspired by his intuitive understanding of the living cell, Hopkins stood self-forgetful in front of the facts. One can see him now, at the top of the stairs, coat open and hands in pockets, backed by his technical assistant, with cigarette drooping over the centrifuge tubes; head quizzically slightly at an angle, benignly smiling, enquiring about the latest results. One never came across anybody at all like him, and now one is sure one never will.

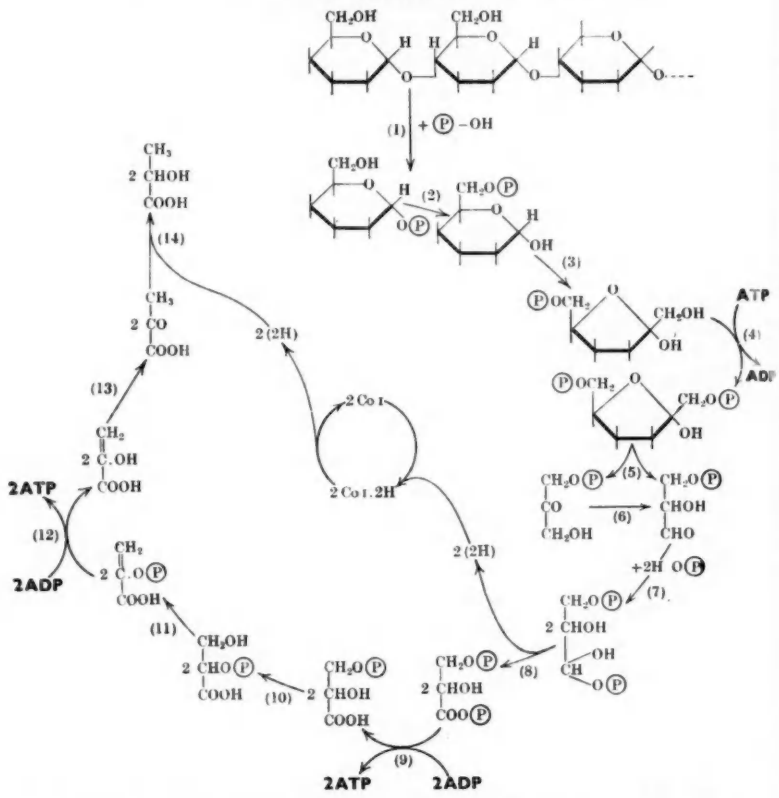
This insistence upon the essentially dynamic nature of intracellular affairs has led in our own time to a new knowledge and understanding of metabolism in relation to physiological function, and in the cells of muscle above all other tissues we are beginning to see a closely integrated picture of the association between chemical composition, intermediary metabolism, and cellular function. In this article an attempt is made to show how, upon the foundations laid by Hopkins himself, our present knowledge has been built.

2. Source of Muscular Energy

Already, in collaboration with Fletcher, Hopkins had provided a starting-point by supplying the first unequivocal evidence that, under anaerobic conditions, muscular activity is associated with the formation of lactic acid. This pioneer work was soon followed by demonstrations from other laboratories of quantitative relationships between work done, heat or tension developed in muscle, and the amounts of glycogen disappearing and lactic acid formed. That glycolysis furnishes the ultimate source of contraction-energy was established beyond doubt. Later, however, Lundsgaard discovered that a muscle, previously poisoned with iodoacetate, is capable of normal contraction without the formation of any lactic acid whatsoever. Iodoacetate prevents glycolysis completely, but does not interfere with the decomposition of phosphagen (creatine phosphate), a normal muscle-constituent discovered about three years earlier by the Eggletons in Britain and by Fiske & Subbarow in the USA. Quantitative relationships between work done and the amount of phosphagen decomposed in iodoacetate-poisoned muscle were next established and, since such a muscle goes into rigor as soon as its supplies of phosphagen are exhausted, it appeared that the hydrolysis of phosphagen is a more-immediate source of contraction-energy than glycolysis itself.

A new mine was sprung when Lohmann showed conclusively that, if phosphagen is added to a dialyzed muscle-extract, it fails to undergo hydrolysis. If adenylic acid is added to the extract, phosphagen breaks down, but not by hydrolysis as had been anticipated. Instead, its phosphate radical is transferred to the adenylic acid, with formation of free creatine and adenosine triphosphate (ATP). Now resting muscle contains ATP but no adenylic acid. It therefore follows that ATP must be decomposed before any breakdown of phosphagen can take place, so that yet another process is interposed between glycolysis, which is the ultimate energy-source, and contraction itself. Englehardt & Lubimowa subsequently discovered that the enzyme catalyzing the decomposition of ATP is identical with the contractile protein of the muscle, myosin, and thus established a close logical connexion between the contractile material of the cell, the enzyme that liberates the contraction-energy, and the immediate source of that energy. In passing, it should be noticed that myosin catalyzes the removal of only one of the three phosphate-radicals of adenosine triphosphate,

FIG. I. SCHEME TO ILLUSTRATE THE REACTIONS INVOLVED IN GLYCOLYSIS*



The part played by phosphagen is omitted for the sake of clarity. The enzymes and coenzymes involved are listed in Table I.

TABLE I. GLYCOLYSIS: ENZYMES, COENZYMES AND INHIBITORS* (see also fig. I)

Reaction	*Enzyme*	*Coenzyme*
1	Phosphorylase	$—PO_3H_2$
2	Phosphoglucomutase	—
3	Oxoisomerase	—
4	Phosphohexokinase	ATP
5	Zymohexase	—
6	Phosphotriose isomerase	—
7	? Spontaneous	$—PO_3H_2$
8	Triosephosphate dehydrogenase	Coenzyme I
9	Unnamed phosphokinase	ADP
10	Phosphoglyceromutase	—
11	Enolase	Mg ions
12	Unnamed phosphokinase	ADP
13	? Spontaneous	—
14	Lactic dehydrogenase	Coenzyme I

* Reprinted from Baldwin, "Dynamic aspects of biochemistry", fig. 28, table 26, by kind permission of the Cambridge University Press.

so that the product is not adenylic acid (adenosine monophosphate) but the corresponding adenosine diphosphate (ADP). This compound, like adenylic acid itself, can be phosphorylated by reaction with phosphagen.

". . . The energy of the muscle", said Hopkins in the address already quoted, "is continuously supplied by the progress of organic reactions, and for a full understanding of events we need to know every detail of their course". As far as anaerobic events are concerned, such a knowledge has been gradually accumulated by the work of many investigators, notably by Meyerhof, Parnas and D. M. Needham, and we are now able to give what we believe to be a fairly complete account of the reactions leading from glycogen to lactic acid in the muscle. The reaction-sequence as we now believe it to take place is summarized in fig. 1. It involves some dozen enzymes and half-a-dozen or more coenzymes. We may well exclaim with Hopkins, "What indeed are we to think of a chemical system in which so great an array of distinct catalysing agents is present, or potentially present?" But, "Underlying the extreme complexity we may discover a simplicity which now escapes us." Hopkins' intuition here, as in so many cases, has been amply justified, this time by the discovery that the molecules of adenosine triphosphate and certain other compounds of phosphoric acid possess some very peculiar properties.

a. Phosphorylation

The ATP molecule can be visualized as consisting of a molecule of adenosine to which are attached in series three phosphate radicals. If the terminal phosphate radical is removed by hydrolysis there is an output of heat amounting to some 12,000 calories for each gram-molecule of phosphate removed. A similarly high yield of energy is obtained if the second linkage is ruptured, but the removal of the last phosphate radical is attended by a comparatively trivial thermal change, amounting in this case to only about 2,000 calories per gram-molecule. Lipmann therefore speaks of the first two phosphate linkages as "energy-rich bonds", as contrasted with the third, an "energy-poor bond", which is typical of phosphate-ester bonds in general. Still more important was the discovery, due in the first instance to Lohmann, that these "energy-rich" phosphate radicals can, under certain conditions, be transferred from one molecule to another, without the loss of any energy whatsoever. Thus, in the presence of the muscle enzymes, phosphagen, which also contains an energy-rich phosphate-bond, can transfer its phosphate radical, together with the energy with which it is associated, to a molecule of ADP so that a new molecule of ATP is produced. Representing the phosphate radical by P and the energy-rich bonds by the special symbol $\sim$, this process can be represented by the following equation (C = creatine):

$$C \sim P + A\text{-}P \sim P = C + A\text{-}P \sim P \sim P$$

Picture now the events following upon the arrival of a stimulus in an iodoacetate-poisoned muscle-cell. In some manner of which we are still ignorant, the muscle myosin gains access to and acts upon ATP, its molecules shortening as it does so, so that the energy of the terminal energy-rich phosphate bonds of the ATP molecules appears largely in the form of mechanical work. The products of the reaction are ADP and free, inorganic phosphate. As fast as ADP is produced it is re-phosphorylated and re-energized at the expense of phosphagen, and this process of alternate decomposition and reconstitution of ATP continues until activity ceases or the phosphagen supplies are exhausted, in which case the muscle goes into rigor. The amount of stored energy-rich phosphate present in the form of phosphagen is four or five times greater than that initially available in the form of ATP, so that phosphagen must clearly be regarded as a device which allows the cell to remain in full activity until glycolysis, which of course takes place in the normal unpoisoned muscle, gets under way. Glycolysis, indeed, is known to be relatively slow in getting started although, once established, it can resynthesize ATP from ADP as fast as, or faster than the reaction with phosphagen. Apart from a few other types, such as the electric cells of certain fishes, only the cells of muscle are normally called upon for sudden response in the form of a very high rate of energy-output, and in all such cells we find that smaller or larger stores of phosphagen are present. Other cells, such as those of yeast and liver, which are characterized by more leisurely forms of activity, use essentially the same glycolytic mechanisms, but contain no phosphagen, and the latter must therefore be regarded as a specialized, adaptive mechanism that tides the muscle-cell over the interval between the onset of activity and the full establishment of glycolysis, an adaptation without which the sustained high level of energy-output so characteristic of muscle could not be achieved.

b. Glycolysis

What now of the glycolytic processes? Examination of fig. 1 shows that for each 6-carbon unit of glycogen broken down to lactic acid, 3 new molecules of ATP are formed from ADP. The synthesis of ATP from a compound of lower energy-content calls for the provision of energy. The chemist, faced with the task of achieving an energy-consuming synthesis, resorts to the use of high temperatures, strong acids, alkalis and other powerful reagents, resources that are denied to the living cell. It follows, therefore, that the reactions immediately preceding the formation of new molecules of ATP must be of fundamental biochemical significance. One of these reactions (reaction 8) consists in a simple dehydrogenation and the second (reaction 11) in a dehydration. The products of these reactions, unlike their precursors, contain energy-rich phosphate bonds, and it is by the transference of these to ADP that the new molecules of ATP are formed. The energy which becomes as it were "concentrated" in the newly-formed energy-rich bonds arises, of course, from the intrinsic chemical energy of the precursors, becoming "concentrated" in the energy-rich bonds as a result of the intramolecular rearrangements catalyzed by the muscle enzymes. Thus, through the reactions of glycolysis, the chemical energy of the stored glycogen of the cell is made available for transfer to ATP, the immediate energy-source of muscular contraction. There is, then, an unexpected simplicity behind the agglomeration of reactions that makes up the glycolytic process, which now appears essentially as a mechanism for the generation of new energy-rich bonds which, by transference to the ADP-ATP system, can be put to physiological service by the cell.

How nicely the metabolism is integrated with the functional needs of the cell can be appreciated from the following considerations. The first energy-significant reaction taking place on the arrival of a stimulus at the muscle-cell consists

in the disruption of ATP by the muscle myosin, the products of the reaction being ADP and inorganic phosphate. The former is promptly re-phosphorylated at the expense of phosphagen, leaving free inorganic phosphate in the milieu. Now, as fig. 1 shows, inorganic phosphate is an indispensable reactant at two points in the glycolytic reaction-chain, viz. at reactions 1 and 7. Glycolysis cannot therefore proceed unless free phosphate is available, but when the cell enters into activity and free phosphate becomes available, glycolysis begins and continues as long as any free phosphate remains. Once activity has commenced, therefore, glycolysis continues and, even when activity has ceased, still continues for a short period, until all the available phosphate has been removed, the normal resting level of ATP has been restored, and the resting stores of phosphagen replenished (see also table I).

c. Oxidation

So far we have considered muscle only under anaerobic conditions. In the more normal state of virtually complete aerobiosis no lactic acid is produced; its immediate precursor, pyruvic acid, is completely oxidized to carbon dioxide and water, instead of being reduced. Our present knowledge of the oxidative processes is far less complete than that of the earlier anaerobic phase, but certain facts have nevertheless been established. Many of the intermediate reactions are known and it has been established that oxidation, like glycolysis, is associated with the generation of new energy-rich bonds and their transference to ADP. Recent estimates put the yield at about 40 to 50 such bonds for each 6-carbon unit of glycogen oxidized, as contrasted with the 3 bonds generated when a similar unit is glycolyzed. This means, in effect, that of the total available energy of the glycogen-store, the muscle enzymes can "capture" about 70 % in the form of ATP when working aerobically.

3. Extramuscular Energy

As has been mentioned, cells of kinds other than muscle also possess most or all of the catalytic equipment involved in glycolysis and oxidation. Here, as in muscle itself, the metabolic degradation of carbohydrate—and there can be little doubt that the same is true of the catabolism of fats—is associated with the generation of new energy-rich bonds and the synthesis of ATP. The question may therefore be asked: why, in cells that do not do mechanical work, do we find catalytic machinery that appears to be uniquely directed towards the synthesis of large amounts of this very peculiar compound? The answer is not far to seek. It is now known that ATP is not the immediate energy-source for muscular contraction alone: on the contrary, it appears to be the essential go-between in all the energy-producing and energy-consuming processes in cells of every kind. Thus, to take but a single example, glucose can be neither metabolized nor stored in the form of glycogen or starch without first being "primed", i.e. raised to a higher energy-level. This process of "priming" is accomplished by the transference of phosphate to the glucose molecule from a molecule of ATP, a reaction that is catalyzed by the enzyme hexokinase. "Priming" is a wasteful process from the energetic point of view, for only some 20 % to 30 % of the energy lost to the ATP system finds its way into the newly-formed molecule of glucose-6-phosphate. Nevertheless, by undergoing an isomerization catalyzed by phosphoglucomutase, the 6-phosphate can be converted into α-glucose-1-phosphate, which is the raw material for the enzymic synthesis of glycogen and starch (reversal of reaction 1). Alternatively the glucose-6-phosphate may be metabolized, but if it goes along the pathway of glycolysis an isomerization is again necessary, followed by a further "priming reaction" to yield fructofuranose-1 : 6-diphosphate (see reactions 3 and 4) before the hexose molecule becomes sufficiently unstable to be split by the enzymes of the cell.

It is a matter of great clinical interest in this connexion that it is to suppression of this "priming" process that the fundamental metabolic breakdown in diabetes mellitus is apparently due. Free glucose cannot be metabolized or stored unless it can first be "primed" by reaction with ATP under the influence of hexokinase. This enzyme is powerfully inhibited by a substance secreted by the anterior pituitary body, which accordingly opposes the storage and metabolism of glucose. Insulin acts by releasing the enzyme from the inhibition caused by the pituitary substance, and the activity of hexokinase is determined by the balance between the concentrations of the two hormones.

The energy-rich bonds of ATP, then, are of manifold importance. They furnish the immediate energy-source for muscular activity and they provide the "priming energy" necessary for the initiation of glucose-metabolism. Very possibly they play a similar part in the breakdown of fatty materials. They provide the energy needed for the synthesis of complex substances such as starch and glycogen from simpler units such as glucose, and there is evidence that they are also involved in the biosynthesis of many simpler compounds such as acetylcholine, glutamine, and hippuric acid. It is believed, moreover, that ATP plays an important part in the performance of the osmotic work necessary for selective absorption of glucose from the alimentary canal, and for its reabsorption from the glomerular filtrate by the renal tubule. It appears to be present and to play an important part in living organisms of every kind and, so far at any rate, no other substance of comparable importance in biological energetics has been brought to light.

* * *

The knowledge and the discoveries so briefly reviewed in this article form but a minute fraction of the harvest gathered in by biochemistry within the last 30 years. That these discoveries, and the detection of so much simplicity behind a welter of detail and apparent complexity, should have been achieved during his own lifetime provides proof enough, should it be needed, of the inspiration of Hopkins' foresight and vision.

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METABOLIC PROCESSES IN MICRO-ORGANISMS

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1 Anabolic processes
  a Fermentation and phosphorylation
  b Cell-building: vitamin needs
  c Mutation: gene-control
2 Metabolic disturbance in the infected host
3 Disturbance of the metabolism of the parasite by chemotherapy

Microbes, particularly bacteria, are unique among biological forms in that study of their metabolic activity preceded the knowledge of their existence. Fermentation and infective disease have both been studied from the earliest times, but the causal agents in both cases awaited the development of the microscope and the master-mind of Pasteur to relate them conclusively together. Pasteur indeed carried this correlation along the first stage of its journey; he believed that both effects were linked with the physiological processes and needs of the causative microbe, but the unravelling of the mechanisms by which the metabolic processes of the cell produced the varying phenomena of fermentation and disease awaited later exploration.

1. Anabolic Processes

Pioneer work in elucidating the biochemical mechanisms by which the microbial cell brings about the chemical events of fermentation was due to Arthur Harden. In his classical studies on the fermentations by *Bact. coli* (Harden 1901) and *B. lactis aerogenes* (Harden & Walpole, 1906) he was the first to make a quantitative study of the products of a mixed bacterial fermentation with the purpose (i) of accounting quantitatively for the substrate fermented in the products of fermentation and (ii) of discovering by what intermediate steps the final stable end-products were produced from the original hexose. He thus laid the foundation on which later workers have built the modern structure of fermentation-chemistry.

a. Fermentation and Phosphorylation

Harden's second piece of pioneering was the discovery that fermentation was linked with the production of phosphate esters (Harden, 1932). It would be hard to exaggerate the importance of this observation; through its development it is now known (Barron, 1943) that all fermentations occur through intramolecular rearrangement, not of 6- and 3-carbon compounds as was thought earlier, but of their phosphate esters through the system of intermediate reactions known as the Embden-Meyerhof-Parnas cycle. This, with minor variations, additions, and modifications, has now been proved to be the scheme into which fit all the ever-growing company of fermentations brought about by bacteria, moulds and other unicellular organisms, including free-living animal cells like spermatoza. In this scheme, the fructose diphosphate discovered and isolated by Harden (1932, p. 58) holds a key position.

But the phosphorylations first studied by Harden have an even more profound biological meaning than that of forming the framework within which fermentations occur. Convergent evidence supplied by several workers (Meyerhof & Suranyi, 1927; Needham & Pillai, 1937) and ably summarized and extended by Lipmann (1941) has shown that the entry of phosphate into the fermentation-cycle results in the formation of phosphate-ester links whose energy content is *c.* 3,000 cal./mol.; and that the result of the changes which occur during the cycle is to concentrate the energy derived from the sugar molecule into an energy-rich bond in phosphopyruvic acid, so that the rupture of phosphate from this substance liberates *c.* 12,000 cal./mol. The fermentation-cycle thus provides the mechanism for concentrating the energy from the carbohydrate molecule into a form from which it can be either liberated or stored within the cell in the energy-rich bonds of adenosine pyrophosphate, whence it can be released to serve the anabolic processes in cell-synthesis. Even chemosynthetic (autotrophic) bacteria appear to work in this way, the energy liberated by the oxidation of sulphur being stored as phosphate esters to be used subsequently for the reduction of CO_2 required in the synthesis of carbohydrate and hence of other cell-material (Vögler & Umbreit, 1942).

b. Cell-building: Vitamin Needs

In retrospect, the mechanism by which the energy-providing systems operate seems comparatively easy to elucidate, as compared with the formidable problem of the building up of cellular material from the substrate. The enzymes and coenzymes of oxidation and fermentation have now all been isolated, and their action in these processes can be followed in full detail in vitro. But between the products of digestion, whether of the animal or microbe, and the final appearance of the new cell, there remained for long a chasm of ignorance. It may fairly be claimed that the study of microbiological chemistry has played a large part in constructing the slender bridges so far thrown across this gulf. This is due largely to the greater tolerance of the microbe towards interference with its metabolic routine as compared with the more-highly-integrated animal organism, and to its much greater tendency to vary biochemically. The microbial cell shows its relationship with that of the animal in requiring for its growth and functioning the entire range of the B vitamins; in fact, several of these, e.g. biotin (Kögl & Tönnis, 1935), inositol (Eastcott, 1928) and *p*-aminobenzoic acid (Rubbo & Gillespie, 1940) were discovered in studies of microbial metabolism before their importance to the animal was recognized.

Many bacteria, yeasts and fungi are able to synthesize every member of the group, but many others, through prolonged cultivation in an environment where these compounds are present (due to the activities of animals, plants or other microbes), have lost certain synthetic powers

and require to have one or more of the vitamins supplied in their media. Such exacting organisms have furnished valuable information as to the function of the vitamin in question; grown on suboptimal concentrations of the factor, the deficient cells display subnormal activities of certain enzymes which—even in non-proliferating cells—function normally when the concentration of the factor is raised. Thus aneurin, or its pyrophosphate (vitamin B_1), was known to be necessary for the oxidation of pyruvic acid by animal tissues and for its decarboxylation by yeasts; similar studies on bacteria by the method mentioned above have shown that it is necessary for other reactions in bacterial metabolism in which pyruvic acid is involved (Hills, 1938). To take another example: the active components of the B_6 complex (pyridoxal phosphate and pyridoxamine) have been shown by this deficient-culture method to form parts of the enzymes catalyzing the transfer of amino-groups from certain amino-acids to certain keto-acids, thus possibly playing a part in the synthesis of proteins, whilst pyridoxal phosphate has been shown to act as coenzyme of the bacterial amino-acid decarboxylases (Gale, 1946). Work on yeast has shown that biotin functions in the assimilation of ammonia (Winzler, Burk & du Vigneaud, 1944), and studies of *L. plantarum* (Stephenson & Rowatt, 1947) have corroborated the observation that pantothenic acid functions in the acetylation of choline. The function of *p*-aminobenzoic acid as a vitamin was foretold through the discovery of its property of antagonizing the action of sulphonamides on bacteria (Woods, 1940). This prophecy was fulfilled within a year when it was shown to be a growth-factor for a strain of *Cl. acetobutylicum* (Rubbo & Gillespie, 1940).

c. Mutation: Gene-control

The work of Beadle & Tatum (1941) in the USA has developed the use of the microbe—principally the mould *Neurospora crassa*—for the study of the biochemistry underlying mutation and gene-control. By the study of artificially-induced mutants they have suggested that each mutant arises by the loss of one gene which controls the production of one enzyme. If one of the enzymes involved in a chain of synthetic reactions is lost by the mutant, then the organism becomes nutritionally exacting towards the product of the step catalyzed by that enzyme. In this way, important information has been gained on the anabolic mechanisms of the cell. For example, it has been shown that anthranilic acid and indole are the serial precursors of tryptophan, the last step in the synthesis being the condensation of indole with serine (Tatum & Bonner, 1944), the same route being independently shown to hold for *Esch. coli* (Fildes, 1945). Similarly, the synthesis of arginine proceeds through ornithine and citrulline (Srb & Horowitz, 1944)[1] whilst the immediate precursors of valine and isoleucine (Bonner, 1946) are the corresponding keto-acids.

The microbe thus supplies ideal biochemical material for the study of anabolic processes, giving results which may prove to be valid also for both animals and plants. It also promises to provide a clue to the mechanism by which the gene controls the production of enzymes and so controls the development of the cell. In the brilliant work of Avery, MacLeod & McCarty (1944) it has been shown that the rough (non-encapsulated) Type II pneumococcus can be transformed permanently into a new type producing the polysaccharide capsule characteristic of Type III. This has been done by incorporating into the growth-medium of the rough form of the Type II organism minute amounts of a rigidly-purified desoxyribonucleic acid obtained by the disintegration of the Type III organism. This transformation seems to be equivalent to the incorporation in the Type II cell of a new gene controlling the enzymic production of the Type III polysaccharide.

[1] [cf. *BMB* 1200, fig. 2.—ED.]

2. Metabolic Disturbance in the Infected Host

So far we have considered problems of synthesis and growth common to all living cells, but medical science is especially interested in the mechanisms by which pathogenic organisms interfere with the metabolism of the mammalian host and cause the onset of disease. It must be admitted that here our knowledge is still fragmentary, but of recent years one or two breaches have been made in the brickwall of our ignorance. Thus certain strains of *Cl. welchii* have been shown to owe their disintegrating action on tissues to three enzymes: (i) a hyaluronidase (McClean, 1941) which disintegrates the polysaccharide hyaluronic acid, the substance forming the intercellular cementing material of tissues, and this disintegration assists the invasiveness of the organism; (ii) a lecithinase which disrupts the surface-membrane of cells and is in fact a cytolytic agent (Macfarlane & Knight 1941); (iii) a collagenase which attacks the collagen sheath of the muscle fibres, leaving behind a friable mass of fibrils with no protection (Macfarlane & MacLennan, 1945). Recent months have also witnessed the isolation in pure crystalline form of two powerful toxins, those of *Cl. botulinum* (Lavanna, McElroy & Eklund, 1946) and *Cl. tetanum* (Pillemer, Wittler & Grossberg, 1946). Both act in amazingly low concentration, L.D.50 (mouse) for the botulinum toxin being 3.2×10^{-5} μg, from which it was computed that the L.D.50 for a man of average weight would be 0.12 μg. This is the lowest concentration in which any poison is known to act. After these achievements it is probable that the disclosure of the mode of action of these toxins will not be long delayed.

Disturbance of the Metabolism of the Parasite by Chemotherapy

One of the most outstanding of recent medical advances has been in the realm of chemotherapy, a rational approach to the study of which was put forward by Fildes (1940); this was based on the idea that chemotherapeutic agents owe their activity to the similarity of their structure to that of essential metabolites whose activity they block by steric hindrance. The discovery that the sulphonamides were antagonized by *p*-aminobenzoic acid (Woods, 1940), later shown to be a growth-factor (Rubbo & Gillespie, 1940), corroborated this view and led to numerous attempts to produce chemotherapeutic agents by synthesizing analogues of other growth-factors and essential metabolites. Many such compounds have been prepared, as for example, analogues of nicotinic acid, pantothenic acid and some amino-acids by the replacement of the –COOH by $-SO_3H$ (McIlwain & Hawking, 1943; Woolley, 1946). These compounds do indeed inhibit the growth in vitro of organisms

which require the factors to which the compounds are structurally related, but so far no chemotherapeutic agents comparable in value to the sulphonamides have been produced by this means.

Another advance in the host-parasite relation comes from a different line of approach. It has long been recognized that non-sporing pathogens cannot long survive in the mixed microbial population of the soil. The mechanism of this biological antagonism was first investigated in a rational manner by Dubos (Dubos & Hotchkiss, 1941), who treated samples of soil with pathogenic cocci over a long period and then examined the population of the treated soil. He isolated an organism, later identified as *B. brevis*, which excretes into its environment a mixture of substances lethal or inhibitory to many other bacteria. Two substances, tyrocidin and gramicidin (Hotchkiss & Dubos, 1941; Hotchkiss, 1946), were isolated as crystalline polypeptides; the former is lethal to most bacteria and appears to act as a cytolytic agent, while the latter is bacteriostatic to gram-positive cocci. This work demonstrated how one organism can antagonize another by the excretion of a substance inhibitory towards the growth of the other. Recognition of this principle and its general exploitation has led to the production in recent years of scores of "antibiotic" substances. Many of these prove generally toxic, but at least two, namely penicillin and streptomycin (Schatz, Bugie & Waksman, 1944), are specifically toxic towards certain bacteria and can be used clinically as chemotherapeutic agents. The discovery of penicillin was an independent development following on the original observation of Fleming (Fleming, 1929) that a mould-colony excreted into the medium something which lysed staphylococcal colonies growing in the vicinity. The instability of the antibiotic proved an obstacle to its large-scale production and purification, but the obstacle was eventually overcome by Florey and his team of workers at Oxford (Chain *et al.* 1940), so that penicillin is now one of the most potent weapons available to medicine.

To the biochemist the chemotherapeutic agents are mainly of interest as tools for the elucidation of growth-processes. The fact that they can be used clinically indicates that they act upon structures, or inhibit enzyme-systems, which are more important to the parasite than to the host, so that the elucidation of their mechanism should assist the development of our knowledge of parasitic existence. All these antibacterial substances prove to be selectively active against certain groups of bacteria; to many, the bacteria loosely classified as gram-positive prove more sensitive than the majority of gram-negative species. It has been found that the staining-complex responsible for the positive gram-reaction is a magnesium-ribonucleotide-complex residing in the surface of the organism (Henry & Stacey, 1943). It has further been found that the gram-positive cell differs from the gram-negative in that the former can assimilate certain amino-acids in the free state and concentrate them within the internal environment prior to metabolism—thus, presumably, compensating for the inability of many of these organisms to synthesize such amino-acids (Gale, 1947; Taylor, 1947). Investigation of the processes whereby the amino-acids migrate across the cell-wall against a concentration-gradient has shown that penicillin-treated cells are unable to assimilate glutamic acid and, consequently, to synthesize protein within the cell (Gale & Taylor, 1946). It has previously been shown that sulphonamides interfere with the metabolism of *p*-aminobenzoic acid and it is now known that this substance forms part of folic acid and other peptides within the cell. We have here, then, indications that the nature of chemotherapeutic interference is beginning to be revealed by the concentrated attacks of biochemistry on the structure and essential anabolism of the growing cell.

One may perhaps summarize the present position by saying that knowledge of bacterial metabolism is fundamental and crucial to the understanding of anabolic processes in general, and that its extended study is the main gateway to a comprehension of the chemical mechanism of infective disease and to the control of this by chemotherapeutic agents.

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WIDER ASPECTS OF STUDIES OF THE NUTRITION OF MICRO-ORGANISMS*

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1 Uniformity of fundamental cell-processes
2 Function of essential metabolites
3 Nutritional approach to bacterial chemotherapy
4 Biosynthesis of essential metabolites
5 Conclusion
References

A complete understanding of the fundamental biochemistry of deficiency-diseases of animals involves the solution of two main problems. First, the precise function of the food-factor (vitamin or essential amino-acid) in cell-metabolism must be established; only in this way is it possible to determine the primary biochemical lesion resulting from lack of the factor, for it is possible that the clinical symptoms arise only indirectly from this lack. Second, the need for such factors implies that the animal in question is unable to synthesize them for itself. But this failure is not common to all organisms; plants and some micro-organisms are able to synthesize a wide variety of the substances required by animals. A detailed knowledge of the biosynthesis of these "essential metabolites" by such organisms may enable the cause of the failure in other organisms to be determined.

The main purpose of the present article is to examine what contribution the study of the nutrition of micro-organisms can make to the solution of these two problems. Work done in recent years suggests that information may be obtained which may have wide application to other cells.

1. UNIFORMITY OF FUNDAMENTAL CELL-PROCESSES

The development of the study of the nutrition of micro-organisms has been outlined by Knight (1945) and Fildes (1946)[1]. Many bacteria require for growth traces of complex organic compounds (essential growth-factors). As these substances were characterized they were found to be already known as vitamins for higher animals (e.g. aneurin, riboflavin, pyridoxin, choline). In recent years there has been an increasing tendency for this order to be reversed; factors first studied as growth-factors for micro-organisms (e.g. nicotinic acid, pantothenic acid, biotin, folic acid, *p*-aminobenzoic acid, strepogenin[2]) have later been found to be important also in animal nutrition.

Some bacteria do not require growth-factors, or perhaps one or two only. Such organisms are found to synthesize the factors not required, or at any rate material with the same biological activity (Knight, 1945; Peterson & Peterson, 1945). It seems a reasonable deduction, therefore, that these factors are required for the normal metabolism of all bacteria and are recognizable as growth-factors or growth-stimulants only when the cell in question cannot synthesize them or can do so only at a suboptimal rate. The inclusive term "essential metabolite" has been proposed (Fildes, 1946) for such substances, which include various amino-acids.

The same essential metabolites are thus found to be required by animal cells and by cells of micro-organisms (bacteria, yeasts, lower fungi, protozoa). Many of them have also been implicated in the nutrition of insects and the isolated root-tips of higher plants (Knight, 1945; Peterson & Peterson, 1945). This uniformity of requirement for certain substances by cells of all types leads to the conclusion that the fundamental cell-reactions in which they are involved may be common to all cells. Thus aneurin or its phosphate esters have been found to function as coenzymes in pyruvate metabolism, e.g. oxidation by pigeon-brain (Banga, Ochoa & Peters, 1939), decarboxylation by yeast (Lohmann & Schuster, 1937), oxidation to acetic acid and CO_2 by *Bact. delbrueckii* (Lipmann, 1944) anaerobic and aerobic breakdown by *Staph. aureus* (Hills, 1938).

It is probable, therefore, that findings concerning the metabolic function of essential metabolites in micro-organisms will, in the main, be applicable to other cells. One important limitation must be noted. Some animal vitamins (notably the fat-soluble group and ascorbic acid) have not so far been found to be concerned in the nutrition of micro-organisms. Such substances may be required for the specialized functions of the differentiated tissues of higher organisms (e.g. vitamin D in calcification).

Micro-organisms have many advantages for the study of essential metabolites. During the stages of purification and identification, the routine biological tests give rapid results and the experimental criterion (growth) is simple to assess. Furthermore, "pure" cultures are used; in tests with animals there is always present, besides animal cells, a considerable bacterial population in the gut. Synthesis of vitamins by gut-organisms may contribute to the nutrition of the animal (Najjar & Barrett, 1945; Daft & Sebrell, 1945) and obscure the results. For later studies of metabolic function, bacterial cells deficient in a given factor may be obtained easily and rapidly by growing in a defined medium containing suboptimal amounts of the factor.

2. FUNCTION OF ESSENTIAL METABOLITES

It is obvious that the main function of essential amino-acids is for the synthesis of cell-proteins. Some, however, also occur in the structure of other growth-factors, e.g. glutamic acid in folic acid (Angier *et al.*, 1946) and unidentified amino-acids in strepogenin (Woolley, 1946b).

* In a general review of this type it seemed undesirable to obscure the text by detailed references to the many hundreds of papers considered either directly or by implication. When possible, therefore, reference has been made to more detailed reviews of particular aspects, or to key-papers from which other references may be traced.

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[1] [*BMB* 929]

[2] For work on strepogenin see Woolley (1946a) and Scott, Norris & Heuser (1947).

Members of the vitamin-B complex have been found to be involved in the structure of coenzymes (or prosthetic groups) of various enzyme-systems. The role of aneurin in pyruvate metabolism has been mentioned above. Nicotinamide appears in the di- and triphosphopyridine dinucleotide coenzymes, and riboflavin in the flavoprotein enzymes, of oxidation-systems (Green, 1941). In the present review, attention will be focussed on other members of the B complex; the examples are chosen to illustrate the general methods of approach available with micro-organisms and the varying degrees of progress made.

General Methods of Investigation

Progress has been made in the main by the use of various combinations of five methods, which are of general application.

A. Discovery that a component of the structure of a coenzyme is identical with, or related to, a known growth-factor.

B. Study of the metabolism of cells deficient in a factor, followed by detailed study of any metabolic process which is affected. It is possible, however, that the effect obtained may be secondary; lack of the factor may affect the synthesis of another factor more directly concerned.

C. Study of the metabolism of the factor itself may provide a hint as to whether it (i) must be built up to a more complex molecule before it can function, or (ii) undergoes some reversible change whilst functioning.

D. The factor may be replaceable in growth-tests by a substance X of a different chemical type. This may suggest that the factor is concerned with the synthesis of X or vice versa.

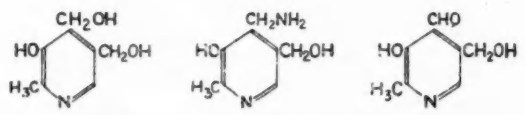
E. Use of substances, often analogues of the factor (anti-metabolite inhibitors, *v. infra*), which may specifically inhibit the utilization of the factor and lead to a breakdown of the metabolic processes with which it is concerned.

The Vitamin B_6 Group

Decarboxylation of amino-acids

The identification of pyridoxal phosphate[3] (fig. 1) as the coenzyme of various amino-acid decarboxylase enzymes of bacteria provides a striking example of the joint application of methods (A) and (B).[4] This work was carried out by Gale and colleagues (mainly A) and by Gunsalus and colleagues (B); it has been fully reviewed by Gale (1946). Cells of the main test-organism (*Str. faecalis* R) deficient in pyridoxin were obtained (*a*) from a medium containing suboptimal amounts of pyridoxin (*b*) from a medium in which pyridoxin was replaced by *dl*-alanine

FIG. 1



pyridoxin pyridoxamine pyridoxal

[3] The position of the phosphate group in pyridoxal phosphate is not yet clear. Recent work (Gunsalus & Umbreit, 1947) appears to exclude the possibility that the phenolic group is phosphorylated.

[4] Capital letters refer to the general methods outlined in the previous section.

(Bellamy & Gunsalus, 1945; Snell, 1945a). An important step forward in this research came from the observation of Snell (1944) that pyridoxal and pyridoxamine had greater growth-promoting activity for some micro-organisms than pyridoxin itself. Further support for the role of the phosphate ester comes from the finding (C) that pyridoxin, pyridoxal, and pyridoxamine can be converted to pyridoxal phosphate by organisms which can use them for growth (Bellamy, Umbreit & Gunsalus, 1945).

Transaminase reactions

Snell (1944, 1945b) suggested that a pyridoxal $\rightleftharpoons$ pyridoxamine transformation might act catalytically in transamination reactions by acting as an intermediate carrier of amino-groups. It has now been found (B) that pyridoxal and pyridoxamine phosphates are both active as coenzyme with cell-free preparations of *Str. faecalis* R, catalyzing transamination between glutamic and oxaloacetic or pyruvic acids (Lichstein, Gunsalus & Umbreit, 1945; Umbreit, O'Kane & Gunsalus, 1946)

e.g. $HOOC(CH_2)_2\ CHNH_2COOH + CH_3COCOOH$

$\downarrow\ \uparrow$

$HOOC(CH_2)_2\ COCOOH + CH_3CHNH_2\ COOH$

Pyridoxamine phosphate is not, however, active as codecarboxylase.

Transamination reactions also occur in animal cells. Here pyridoxal phosphate has now been found to act as coenzyme with the glutamic-aspartic and glutamic-alanine transaminases (Braunstein, Kritzmann, Gale, Tomlinson & Samarina, 1946; Ames, Sarma & Elvehjem, 1947).

Metabolism of tryptophan

The final stage in the synthesis of tryptophan by the mould *Neurospora* is the condensation of indole and serine (see p. 311). Pyridoxal phosphate acts as coenzyme in this condensation (Umbreit, Wood & Gunsalus, 1946). There is also evidence (see p. 312) that pyridoxin derivatives are involved in the synthesis of tryptophan by *Lactobacillus arabinosus* (Schweigert, 1947). On the catabolic side, pyridoxal phosphate has been found to be one of the coenzymes involved in the breakdown of tryptophan to indole by *Esch. coli* (Dawes, Dawson & Happold, 1947; Wood, Gunsalus & Umbreit, 1947).

With animals it is found that pyridoxin-deficient rats (B) fed with tryptophan excrete xanthurenic acid (an abnormal product). Feeding of a desoxy-analogue (E) of pyridoxin (which presumably inhibits the function of pyridoxin) leads to excretion of the same acid by both normal and deficient rats (Lepkovsky, Roboz & Haagen-Smit, 1943; Porter, Clark & Silber, 1947).

Synthesis of other amino-acids

With certain species of *Lactobacilli*, the growth requirement for several amino-acids is abolished if pyridoxin is present (D). In some cases CO_2 is also necessary. Where tested, pyridoxal and pyridoxamine were more active than pyridoxin. Since organisms growing under these conditions were shown to synthesize the amino-acids in question, it appears that pyridoxin plays an essential part in their synthesis (Stokes & Gunness, 1945; Lyman *et al.*, 1947).

Conclusions

Work with bacteria shows that the biologically-active forms of pyridoxin are pyridoxal and pyridoxamine phosphates. These compounds appear to have a general coenzyme function in amino-acid metabolism (both breakdown and synthesis) and there is some evidence for a similar role in animals.

Pantothenic acid

McIlwain (1946) has studied this factor mainly by methods (B), (C) and (E). He finds that pantothenate is metabolized (concurrently with glucose-fermentation) by organisms requiring it for growth. This metabolism is inhibited by the same pantothenate analogues (e.g. pantoyltaurine) which inhibit growth, and appears to be connected with growth-factor function. It is suggested that the metabolism may yield a substance which is essential for growth. The necessity for a coupled energy-yielding reaction suggests the formation of a more complex molecule, and this may be consistent with the finding of Lipmann *et al.* (1947), that the coenzyme for the acetylation of choline by brain-tissue is a pantothenate derivative from which pantothenate may be liberated by enzyme treatment. Stephenson & Rowatt (1947) also find that pantothenate is required for the acetylation of choline by a strain of *Lactobacillus plantarum*; suspensions of deficient cells had low activity which was much increased by pantothenate (B).

Pantothenate-deficient cells (B) of *Proteus morganii* show decreased aerobic and anaerobic metabolism of pyruvate (Dorfman, Berkman & Koser, 1942; Hills, 1943). There are also findings (D) that the tryptophan requirement of *Staph. aureus* can be met by pantothenate plus glucose (Sevag & Green, 1944), and the pantothenate requirement of *Cl. botulinum* by aneurin plus choline (Lamanna & Lewis, 1946). It is possible that pantothenate is concerned with a key-reaction (involving acetylation or acetate metabolism?) common to these systems.

Biotin

Several studies implicate this factor in nitrogen metabolism. Biotin-deficient cells of *Saccharomyces cerevisiae* have greatly-depressed rates of respiration and fermentation (B), and these are raised by biotin plus ammonia, but not by either alone. Assimilation of ammonia from the medium by such cells was found to depend on the presence of biotin (Winzler, Burk & du Vigneaud, 1944). There is evidence (D) that biotin is involved in the synthesis of aspartic acid, since (*a*) the stimulating effect of biotin on the growth of *Torula cremoris* can be partially replaced by this amino-acid (Koser, Wright & Dorfman, 1942), and (*b*) the aspartic-acid requirement of certain lactic-acid bacteria is abolished if sufficient biotin is present. Organisms growing with biotin alone were found to contain as much aspartate as those actually grown with aspartate. Since some biotin is required even when aspartate is supplied, it follows that synthesis of this amino-acid is not the only function of the factor (Stokes, Larsen & Gunness, 1947).

***p*-Aminobenzoic Acid**

The role of *p*-aminobenzoic acid as an essential metabolite was predicted from its properties in overcoming the inhibition of bacterial growth by sulphonamide drugs (Woods, 1940). The prediction has been fulfilled by the discovery of many micro-organisms which require this substance as an essential growth-factor (see Knight, 1945; Woods, 1947). It has also been implicated in animal nutrition (Ansbacher, 1944). Elucidation of the metabolic function of *p*-aminobenzoic acid should therefore throw further light on the fundamental mode of action of the sulphonamides. The original hypothesis suggested that the sulphonamides inhibit competitively enzyme-reactions involved in the utilization of *p*-aminobenzoic acid by the cell, and considerable information as to the nature of these reactions is now available. Since sulphonamides are inhibitors of the utilization of this factor, method (E) has yielded much information. Method (D) has been applied to organisms (including induced mutants) requiring *p*-aminobenzoic acid for growth, and has also been very helpful. It is possible in the space available only to summarize the present position, but a more detailed analysis of the evidence and full references are given by Woods (1947).

Folic acid is another essential metabolite for micro-organisms (and for higher animals), and the molecule is now known to contain a *p*-aminobenzoic-acid residue. Within a limited group of bacteria, requirement for folic-acid synthesis appears to be the only function of *p*-aminobenzoic acid, and to be the only point of inhibition by sulphonamides. With other bacteria, however, there is evidence that this factor is also involved in the synthesis of purines, thymine and methionine, and that sulphonamides also inhibit these functions. With the nucleic-acid derivatives it is possible that the effect occurs through the intermediate production of folic acid, but with methionine the mechanism is unknown. It may be noted that various purines and pyrimidines and methionine are also essential metabolites, and appear as growth-factors for many micro-organisms.

3. NUTRITIONAL APPROACH TO BACTERIAL CHEMOTHERAPY

The development of the idea that the action of drugs may be due in some cases to inhibition of an enzyme, and that this inhibition occurs by virtue of a structural relationship between the drug and the natural substrate, has been discussed by McIlwain (1943), Woolley (1946c) and Roblin (1946). The discovery that *p*-aminobenzoic acid overcomes the inhibition of bacterial growth by sulphonamides (to which it is structurally related) and that it is an essential metabolite for bacteria (*v. supra*) has stimulated a search for analogues of other essential metabolites which might inhibit bacterial growth in a similar manner. It was hoped that such substances (often called metabolite antagonists) might also prove to be useful chemotherapeutic agents (Fildes, 1940a). A large number of such compounds has now been tested and many of them inhibit the growth of various bacteria, usually species which require the metabolite in question as a growth-factor. On the other hand, only one or two substances with appreciable therapeutic value have so far been obtained (Roblin, 1946; Woolley, 1946c, 1947). Many other properties besides capacity to inhibit bacterial growth will determine the therapeutic value of a substance (McIlwain, 1944); amongst these are

the rates of absorption, excretion and possible destruction by the tissues of the host-animal. Furthermore, the bulk of these metabolite antagonists have been modelled on substances which are equally as important for the host-cells as for the micro-organisms (see p. 308) and are likely to inhibit important metabolic processes of both (absorption. etc. being equal). Indeed, characteristic symptoms of the corresponding vitamin-deficiency disease have been found to follow the administration to animals of several of these inhibitors (Woolley, 1946c).

In the control of bacterial infections it may often be sufficient to prevent growth for a limited period whilst the defence-mechanisms of the host cope with the situation. In these circumstances, a short-term interruption of cell-multiplication processes is less likely to do harm to the adult host than to the bacterium. It is possible, therefore, that the metabolite-antagonist approach would yield a higher dividend if it could be applied to essential metabolites more specifically concerned with cell-division, but this must await the characterization of such metabolites.

Apart from possible applications to chemotherapy, metabolite-analogues have been used with much profit as specific inhibitors in fundamental biochemical studies. A number of examples of this has been given in other sections of this review.

4. BIOSYNTHESIS OF ESSENTIAL METABOLITES

It has been pointed out (p. 308) that substances recognized as growth-factors for particular micro-organisms are probably essential for the growth of most micro-organisms, the difference being that some organisms can achieve their synthesis whilst others cannot. If a number of organisms require the same growth-factor, the power to synthesize it may have failed with different organisms at different stages of the series of reactions by which the synthesis is accomplished; the provision of intermediates above the point of failure will enable the synthesis to be completed and the organism to grow. Thus ammonia, nicotinic acid, nicotinamide and nicotinamide-riboside have been proposed as intermediates in the synthesis of phosphopyridinedinucleotide coenzymes, since a series of organisms exists in which each of these substances is the simplest molecule which will support growth in the absence of the higher forms (Knight, 1945). Similar evidence can often be obtained with a single species if a number of strains or mutants, each requiring the same growth-factor, are available for study. The outstanding work of Beadle (1945) and his colleagues with induced mutants of *Neurospora* has proved the value of this technique. By *x*- or ultra-violet irradiation of this mould, a number of "biochemical" mutants were obtained, each differing from the parent in requiring one further growth-factor. Similar mutants have been obtained by treatment with mustard-gas or its nitrogen analogue (Horowitz *et al.*, 1946). Mutants requiring most members of the vitamin-B complex and a number of amino-acids have now been isolated. These mutants are genetically dissimilar from the parent-strain and from one another, which suggests that the synthesis of individual metabolites is controlled by distinct genes. In a number of cases (e.g. tryptophan, arginine) two or more genetically-dissimilar mutants requiring the same factor have been found, and analysis of response to possible intermediates has shown that the synthesis has broken down at different points. Thus, individual steps in the synthesis of a growth-factor may be controlled by different genes.

Analogous biochemical mutants of bacteria have been obtained by similar treatments and by the action of bacteriophage (Roepke, Libby & Small, 1944; Tatum, 1945; Lederberg & Tatum, 1946; Anderson, 1946). With bacteria there can be no genetic analysis, and therefore no hint as to which of a number of mutants requiring the same factor are likely to be biochemically dissimilar in detail.

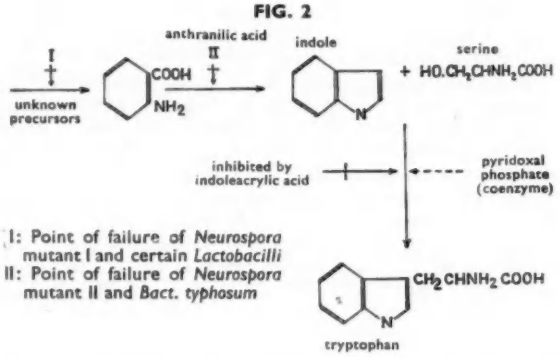
If an exacting organism is grown in the presence of the growth-factor required, the intermediate compound corresponding to the point of failure of the synthetic chain is sometimes formed and accumulates in the medium. Thus a nicotinamide-requiring mutant of *Neurospora* produces a substance (probably an oxypyridine carboxylic acid) which promotes the full growth of another, but genetically distinct, mutant, and is therefore probably an intermediate in the synthesis of nicotinamide (Bonner & Beadle, 1946). Accumulation of precursors may also occur when growth is limited by specific inhibitors of the utilization of a metabolite (Fildes, 1945). Such growth-inhibitions may, if competitive in nature, yield further information; addition of the product of the inhibited reaction should promote growth irrespective of the concentration of the inhibitor, or (Shive & Macow, 1946) may raise the concentration of inhibitor required if the latter also affects other reactions.

This nutritional approach to problems of biosynthesis is as yet in its infancy, but shows great promise. Limitation of space precludes a full account of its application, but the case of tryptophan will be examined since it illustrates well many of the above points.

Tryptophan

Evidence that anthranilic acid and indole are intermediates in the biosynthesis of this amino-acid was first obtained from observations that the tryptophan requirement of *Bact. typhosum* could be met by indole, and that of *L. arabinosus* and *L. casei* by indole or anthranilic acid (Fildes, 1940b; Snell, 1943). Tatum & Bonner (1944) then isolated two genetically-distinct mutants of *Neurospora*, each requiring tryptophan. Mutant I also grew if given indole or anthranilic acid, but Mutant II responded only to indole. Furthermore, anthranilic acid accumulated when Mutant II was grown in the presence of tryptophan or indole. The role of anthranilic acid and indole as intermediates was therefore confirmed and their order of formation established (see fig. 2). It was next found that tryptophan was produced if washed mycelium of Mutant II was incubated with indole and serine. The final stage of the synthesis is thus the direct condensation of indole and serine; pyridoxal phosphate has since been shown (see p. 309) to act as coenzyme in this reaction. Additional evidence that the scheme given in fig. 2 applies also to bacteria has been obtained by different methods. 3-Indoleacrylic acid inhibits the growth of bacteria and the inhibition is overcome non-competitively by traces of tryptophan; this substance is therefore a specific inhibitor of tryptophan synthesis. A strain of *Bact. typhosum* (trained to grow without either indole or tryptophan) was found to accumulate indole in the medium when growth was partially suppressed by indoleacrylic acid; furthermore, inhibition

FIG. 2



of growth was much reduced if serine were added (Fildes, 1945). The growth-response of *L. arabinosus* to indole has been studied by Schweigert (1947) with an amino-acid medium not containing serine. Growth was poor unless both serine (or acetate) and derivatives of pyridoxine were added. A response equivalent to that given by tryptophan was finally attained in a medium containing pyridoxin, serine and acetate; the function of acetate is not clear. Since anthranilic acid did not promote full growth even in a casein-digest medium supplemented with pyridoxin and acetate, it follows that other substances are involved in the conversion of anthranilic acid to indole.

The final stages in the biosynthesis of tryptophan by micro-organisms are thus established with reasonable certainty and in some detail. Outstanding problems are the precise mechanism of the anthranilic-acid—indole conversion, and the nature of the precursors of the former substance. The observation (Sevag & Green, 1944) that pantothenate plus glucose can replace tryptophan for *Staph. aureus* may have some relation to these problems.

5. CONCLUSION

The purpose of this review has been to illustrate the contribution which studies of the nutrition of micro-organisms can make to several outstanding problems of general cell-nutrition. It is not suggested that this is the only approach, and it is clear that the results should not be taken to have general application to all cells until confirmatory evidence has been obtained. Apart from the intrinsic interest to microbiological chemistry, it does appear, however, that information obtained by relatively-simple techniques with micro-organisms may give a valuable directive for similar types of research with other cells.

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DEVELOPMENT AND THEORETICAL SIGNIFICANCE OF BRITISH ANTI-LEWISITE (BAL)

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1 Biochemical lesions and the pyruvate-oxidase system
2 Arsenical researches
3 Further theoretical points
4 General implications
References

British Anti-Lewisite (BAL) is the name given in the USA to 2:3-dimercaptopropanol, which was developed in Oxford during the first 18 months of the war as an antidote to the arsenical vesicants (see Peters, Stocken & Thompson, 1945) [47 71 74]. In this account, the threads which were woven into the pattern of the final research will be sketched and some details of the behaviour of BAL itself, and of its theoretical significance, will be included. The therapeutic applications in medicine are being treated elsewhere[a] (Thompson, 1947)[64].

Some general remarks will clarify the subsequent account; (i) Very broadly, there are three kinds of toxic arsenicals, viz. arsenite, the therapeutic arsenicals such as arsphenamine OH⟨⟩As = As⟨⟩OH (NH_2 NH_2) and compounds of significance for chemical warfare such as diphenylchloroarsine and lewisite ($CH.Cl : CH.As Cl_2$). It is a reasonable view[69] that the toxicity of arsphenamine is due to the oxidation-product, the trivalent arsenoxide[b] OH⟨⟩AsO (NH_2). (ii) Much of our work has been concerned with SH groups, which, following theoretical suggestions of Heffter & Arnold, were the subject of extensive research by Gowland Hopkins (1921, 1929) [25 26], who first isolated the SH compound—glutathione—which is present in the tissues, and demonstrated its properties; in particular, it may be noted that the characteristic purple reaction with sodium nitroprusside and ammonia is given not only by soluble substances in the tissues, but also by SH groups linked to insoluble proteins such as skin and boiled muscle-tissue, the so-called "fixed SH groups". (iii) Lastly, it should be made clear that chemical-warfare agents, in concentrations which are profoundly toxic to cells, are not general protoplasmic precipitants. Their action is much more subtle.

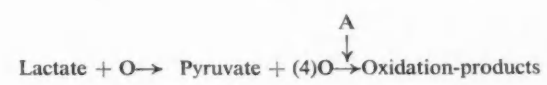
[a] [*BMB* 1199]
[b] L. Pauling has told the writer that he considers that the usually-accepted formula is not correct.

1. Biochemical Lesions and the Pyruvate-oxidase System

At least two events give rise to a blister of the skin: the initial biochemical lesion, and the more complex pathological response following in its train. The development of the antidote depended upon knowledge of the initial biochemical lesion[c], and has been a curious mixture of planned and unplanned research. As much of the work involved the use of the pyruvate-oxidase system, it is appropriate to recall briefly some of our work upon the biochemical lesion in vitamin-B_1 deficiency[39]. By this term is meant the initial change in tissue-cells which precedes any damage visible with the microscope. For many years we studied in this connexion the condition of opisthotonus in the rice-fed pigeon due to vitamin-B_1 deficiency, a condition which is completely reversible in 30 minutes or less by appropriate injection of the vitamin (for review see references 40, 42). After ten years' work, it was proved (Banga, Ochoa & Peters, 1939)[3] that this convulsive condition is solely due to lack of the co-factor (aneurin- or thiamin-pyrophosphate)[d] in the brain-tissue, with a consequent interruption of carbohydrate degradation at the stage of pyruvate; energy-giving reactions therefore fail. Some of this research was used in the war-work.

Turning to a few details: the research rested upon the discovery of the specific action in vitro of vitamin B_1 upon the avitaminous brain in the presence of pyruvate ($CH_3.CO.COO-$), or a pyruvate-yielding substrate; most of it involved observation of the respiration in vitro of mashed pigeon-brain tissue, called "brei", in which all outlines are destroyed, but nuclei remain mainly intact. The diagram (fig. 1) indicates the course of the reaction for brain-tissue respiring in vitro in lactate solutions of pH 7.35.

FIG. 1



In this reaction about two-thirds of the pyruvate is completely burned to $CO_2 + H_2O$; the remainder is lost mainly by a side-reaction to acetate. Lack of aneurin-pyrophosphate interrupts the reactions at A, leading to accumulation of pyruvate in vitro[48], and in vivo to large increases in the content of pyruvate in the blood in the final stage of the deficiency[65]. It is the only known biochemical difference between the brain of the convulsing pigeon and the normal brain.

2. Arsenical Researches

For proper perspective, it may be recalled that arsenicals were first used as toxic smokes in World War I; working under J. Barcroft, the writer well remembers the active research engendered by this, and at that time an attempt was made (McCleland & Peters, 1919)[32] to get some rules for the toxicity of such trivalent arsenicals to ciliates; in addition to the finding that aromatic compounds were more toxic than aliphatic, there emerged the important point that the oxides formed by hydrolysis were at least as toxic

[c] A term introduced by Gavrilescu & Peters (1931)[31].
[d] Also called cocarboxylase.

as the corresponding chlorides. Arsenical compounds, after penetrating the skin as chlorides and hydrolyzing in contact with aqueous phases in the tissue, are still toxic, which is an important distinction from mustard-gas. About this time (1917) lewisite was discovered in the USA; as subsequent events showed, it was a highly significant substance.

Our researches in World War II for antidotes to the war gases were based upon two ideas: (i) that an SH group was attacked by the As[e] and (ii) that this was a constituent of the pyruvate-oxidase system. The work leading to these ideas will be briefly traced.

SH Groups and Arsenicals

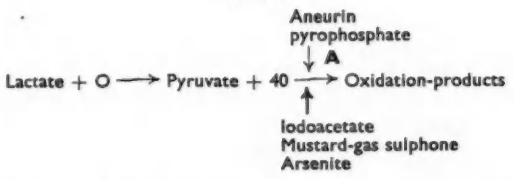
Following the work at Porton in World War I, the writer undertook fundamental investigations in the Chemical Defence field, and E. Walker came to help him. It was found that mustard-gas sulphone[50] stopped the glutathione catalysis of muscle-tissue just then described by Hopkins & Dixon (1922)[27]; as a fixed SH group is part of this system, there followed the finding that several vesicants abolished the reaction for this in muscle, skin and trachea, and that this occurred not only with the sulphone mentioned but also with diphenylchloroarsine and allyl isothiocyanate. At this stage we were much interested by the appearance of work upon therapeutic arsenicals by Voegtlin, Dyer & Leonard (1923)[68], in which they showed that arsenoxide combined with glutathione in SH form, and that monothiol compounds in rather large excess protected against the toxicity of the arsenical. This led[f] to a test, with good effect, of the protective action of the monothiol thioglycollic acid and of monothioethylene glycol against diphenylchloroarsine in ciliates, and to some evidence for reversal of toxicity. Though convinced then of a connexion between the toxicity of these arsenicals and mustard-gas sulphone[g] and a combination with SH groups, a conviction also shared by Voegtlin (1925)[67] for the therapeutic arsenicals, our research was discontinued in 1926, largely owing to the lack of information as to the significance of the sulphur system.

Meanwhile, this connexion was strengthened by other work which was continued in relation to the therapeutic arsenicals, especially by Voegtlin's group and by Eagle (1939)[18]; Rosenthal (1932)[54] also found indirect evidence for the combination of arsenoxide with the SH groups of denatured albumen. During this time, also, it was shown (Cohen, King & Strangeways, 1931)[8] that thioarsinites were dissociated in alkaline solution, e.g. the equation $R.AsO + 2R'SH \rightleftharpoons RAs(SR')_2 + H_2O$ was reversible; an observation which we thought was a valuable pointer to the possibility of therapeutic reversal.

Pyruvate-oxidase System and Arsenicals

The idea that chemical-warfare agents attacked cell-enzymes was early mooted[20], though no proof was given, nor could we get evidence for this[50]. During the vitamin-B_1 researches, however, an observation was made which to the writer[40] reopened the whole question of enzymes in relation to the problem. We had found (fig. 2) that

FIG. 2



iodoacetate interfered positively at A in a *normal* pigeon-brain brei in a similar way to the negative interference produced by vitamin-B_1 deficiency; both led to accumulation of pyruvate from lactate (Peters, Rydin & Thompson, 1935)[44]. The important fresh point was that small concentrations of mustard-gas sulphone (0.09×10^{-5}M.) acted similarly; since other enzymes concerned in the brei (i.e. the cytochrome-system) were by inference unaffected, this experiment indicated a selective action of the poison upon the pyruvate-oxidase system. Iodoacetate is a weak vesicant; hence a causal connexion was suggested between the selective enzyme-attack and the biochemical lesion leading to vesication. About the same time, this was extended by the observation that minute amounts of arsenite (see reference 45) had a similar action[h]. The analogy with iodoacetate was especially interesting because work at that time in 1932–33 [11 51 53] had led to the view that inhibitions produced by it were due to interaction with SH groups. Combined with the earlier observations upon arsenicals, it led to the suggestion that various poisons attacked an SH group in the pyruvate-oxidase system[41].

Very early in World War II, after retesting some of these points, the writer felt prepared to initiate, defend and direct a programme of extramural research for the Ministry of Supply with the object of reaching antidotes for mustard-gas and lewisite based upon the two ideas presented above, and upon confidence in those around him in his laboratory. The matter is put this way intentionally; though biochemists have a natural faith in enzymes, and though we had then proof of the profound pathological effect of failure of cocarboxylase in vitamin-B_1 deficiency, the idea that toxic effects upon an enzyme could initiate such a complicated process as vesication was not then at all acceptable in physiological and medical circles, or in those of pure chemistry; nor was it thought likely that any poisoning could be reversed. One can well understand the hesitation felt, especially when in addition the reservation of personnel in war was in question.

The team who embarked upon this work were roughly divided so that at the start H. M. Sinclair & R. H. S. Thompson worked upon arsenical substances, and E. R. Holiday, A. G. Ogston, J. St.L. Philpot, L. A. Stocken & R. W. Wakelin upon mustard gas; but the work went forward as a whole, and there was constant discussion by all of the research group. After some ten months, Sinclair and Philpot left for other work; but later V. P. Whittaker and G. H. Spray joined.

It was soon confirmed that, among several enzymes examined, the pyruvate-oxidase system was by far the most

[e] A nitrogen group could not be absolutely excluded at that time, but was thought unlikely.
[f] Walker, E., 1925 (published 1928)[70].
[g] Mustard-gas itself is an exception[45].
[h] Krebs (1933) had previously claimed a specific effect upon α-keto-acid oxidase; his concentrations of As were however too large to settle this[39].

sensitive to lewisite and arsenite (Peters, Sinclair & Thompson, 1946)[45]. We also got more evidence for the presence of an essential SH group, because the enzyme system was inhibited by maleate and -S-S- compounds[49]. Both of these reagents had been introduced by Hopkins and his school[38 37] for the detection of SH enzymes. Succinodehydrogenase is also present in brain brei and is an SH enzyme[14]; but it is less sensitive, so that at low concentrations of the arsenical, there is selective poisoning of the pyruvate-oxidase system[i]. Hence pyruvate should accumulate in the blood of an animal poisoned with these arsenicals, as happens in vitamin-B_1 deficiency. Table I shows that there is an increased concentration in the blood after poisoning with As.

TABLE I. EFFECT OF INJECTED ARSENITE ON THE BLOOD-PYRUVATE LEVEL OF PIGEONS

(Expressed as mg. pyruvic acid/100 g. blood, as determined by 24-dinitrophenylhydrazone method. Duration of intoxication given in parentheses.)

	Normal	Acute	Chronic	Total dose As_2O_3 (mg.)
	1.28	4.02 (2 hr.)	12.39 (4 days)	8.5
	0.94	3.00 (2 hr.)	14.15 (4 days)	8.5
	0.94	3.12 (2 hr.)	13.85 (43 days)	7
		6.30 (3 hr.)		
Average	1.06	4.11	13.47	

Similar results were obtained for bisulphite-binding capacity (B.B.S.) of the blood in pigeons, and for pyruvate and B.B.S. with arsenite and lewisite in rats.

Data of Peters, Sinclair & Thompson, 1946[45]

This formed the background for the use of the pyruvate-oxidase system as an enzyme for in vitro tests of arsenical antidotes, and it has never failed. Evidence was also produced (Thompson, 1946)[63] that pyruvate oxidation in skin was inhibited by lewisite. Nevertheless, at this stage there were still facts difficult to fit with the main ideas; perhaps the most serious of these was the complete failure to protect animals or even the brain-enzymes against the toxicity of these arsenicals (Sinclair, 1940)[55] by large concentrations of monothiols, a somewhat different finding from that of the Voegtlin school for arsenoxide. In the early summer of 1940, the war-situation was more serious; this meant a sharpened scepticism as to the value of enzyme research as a contribution to the war-effort, which finally led to the official discontinuance of the enzyme work; nevertheless the arsenical research was continued upon the basis of looking for possible specific antibodies to arsenical proteins which might be formed by lewisite[j]. It should be realized that during all this year thiol-compounds were being made (mainly by L. A. Stocken) in relation to the mustard-gas work; though the more obvious avenues in the arsenical work were now narrowing, there was still left the systematic study of the relative dissociation of various thioarsinites, often urged by Philpot; however the crucial experiment came differently. In connexion with the research into the arsenical "immune proteins", our colleagues Stocken & Thompson (1946a)[59] started to make, and analyze for As-content, arsenical compounds of kerateine (Goddard & Michaelis, 1934)[33], which is a reduced keratin, rich in SH groups. For lewisite-kerateine compounds made under biological conditions of pH and at room-temperature, it was found that from lewisite the amount of arsenic taken up in combination was limited; it was not increased by exposure to a considerable excess, and in great part the amount combined was conditioned by the presence of

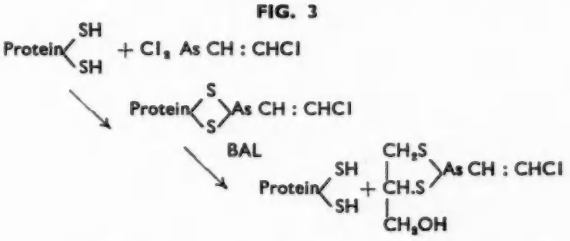
TABLE II. ANALYSIS OF ARSENIC DERIVATIONS OF KERATEINE AFTER EXPOSURE TO EXCESS OF THE ARSENICAL

Substance	Arsenical	S %	As %	
kerateine	lewisite	1.36	0.58	
		—	0.48	
		1.32	0.63	
		1.41	0.46	
		1.31	0.47	
		—	0.53	
			0.52 %	mean
	sodium arsenite		0.41 %	mean (4 experiments)
metakeratin	lewisite	1.22	0.04	
		1.37	0.07	
			0.05 %	mean

Data of Stocken & Thompson, 1946a[59]

-SH groups as such. With metakeratin, in which the SH groups have been oxidized to SS, the amount of As combined is no more than that from arsenate—about 0.05 %. The lewisite-kerateine was resistant to reprecipitation and dialysis. Most important of all, more -SH groups disappeared than As atoms bound by the kerateine; from this, there followed the conclusion that some 75 % of As must be bound in ring form with the protein SH. Since ring compounds would be expected to be a more stable combination, there emerged the "dithiol" theory (Stocken & Thompson), according to which the special stability of this enzyme "thio-arsenite" was due to the presence of two -SH groups upon a component of the enzyme so placed that a ring could be formed with a trivalent arsenical. It could be surmised that if a suitable dithiol could be found, able to form a more stable compound, as in fig. 3, it would

FIG. 3



reverse the combination with the tissue-protein. After preliminary trial of two dithiols, the new compound 2 : 3-dimercaptopropanol was synthesized (Stocken, 1947)[58]; ultimately this was called BAL (British Anti-Lewisite) by the workers in the USA—a courteous gesture; so nearly allied to glycerol, this substance has excellent penetrant properties for skin.

[i] It is interesting to note that the total oxidase-system is more sensitive to arsenite than the pyruvate-dehydrogenase component.[45]

[j] All credit should be given to Mr. J. Davidson Pratt (and the Ministry concerned) for taking the responsibility of active support at this stage.

Synthesis of 2 : 3-*dimercaptopropanol* (*BAL*)

$CH_2:CH.CH_2OH$

$\xrightarrow{B_{r_2}} CH_2B_r.CH\ B_r.CH_2OH$

$\xrightarrow{NaSH} CH_2.SH.CH.SH.CH_2OH$

It is indeed a curious coincidence that the first new compound[k] made should be so efficient and also the least toxic in this series. Several dithiol compounds were subsequently made in Oxford and in Canada[74] and a large number in the USA[71]; none proved less toxic. The LD_{50} (dose killing 50 % of a given batch) for rats is about 120 mg./kg.

The behaviour of BAL will now be briefly described. The compound lewisite-BAL is so stable that it gives no nitroprusside reaction. When added to a brain brei before addition of lewisite, BAL protects the pyruvate-system (Table III), in marked contrast to the monothiol compound.

TABLE III. BRAIN PYRUVATE-OXIDASE (BREI) AS TEST-SYSTEM FOR ARSENICAL ANTIDOTES (PROTECTIVE ACTION OF DITHIOLS)

Antidote	Inhibition of O_2 uptake					
	Lewisite			Lewisite + thiol		
	0–30′	30–60′	60–90′	0–30′	30–60′	60–90′
Dithiol compounds						
toluene 3 : 4-dithiol ...	67	59	59	0	0	0
ethane 1 : 2-dithiol ...	56	53	50	0	0	0
2 : 3-dimercaptopropanol	72	46	46	0	0	0
1 : 3-dimercaptopropanol	45	47	43	0	2	2
1 : 3-dimercaptopropane	49	52	50	0	0	0
2 : 3-dimercaptopropylamine	45	48	49	0	9	17
kerateine (0.3 %)	65	52	54	10	8	17
Monothiol compounds						
monothioethyleneglycol	57	55	—	54	55	—
cysteine HCl	48	56	—	51	56	45

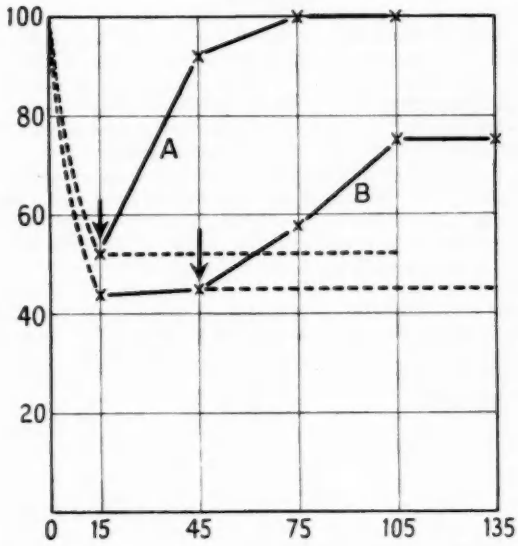
The thiol was added immediately before the lewisite. The effects in successive respiration-periods are given separately. Data of Stocken & Thompson (1946b)[60]

According to the theory outlined in fig. 3, it should also reverse the toxicity when established. Fig. 4 shows that this takes place, and adds the further points of interest that the reversal is not instantaneous and that delay in adding the antidote may lead to some irreversible damage.

Turning now to the effect upon skin in vivo, the photographs (fig. 5–6) show the antidotal action in man. Fig. 5 was taken 2 hours after applications of 1 mm. drops of lewisite at A, B and C. The right arm was treated with antigas ointment after 5 minutes at A, and after 2 hours at C; the left arm was treated with BAL at corresponding times; B was the untreated control. Fig. 6, taken 24 hours after contamination, shows that antigas ointment and BAL were equally effective after 5 minutes, but that after 2 hours only BAL prevented the blister. Indeed at 2 hours after contamination, there is usually erythema and often commencing oedema. The condition is reversed by the antidote and not by a monothiol compound. Remarkable

[k] Independently another preparation of this compound was later published.[65]

FIG. 4. REVERSAL OF TOXICITY TO PYRUVATE OXIDASE



Reversal by BAL of toxicity to the pyruvate-oxidase system induced by addition of sufficient lewisite to give 50 % inhibition of the respiration (approximately 17 μM). (From data of Stocken & Thompson, 1946b)[60]

↓ : BAL added to system
A: 15′ poisoning
B: 45′ poisoning
Abscissae: Time (min.)
Ordinates: Respiration (%)

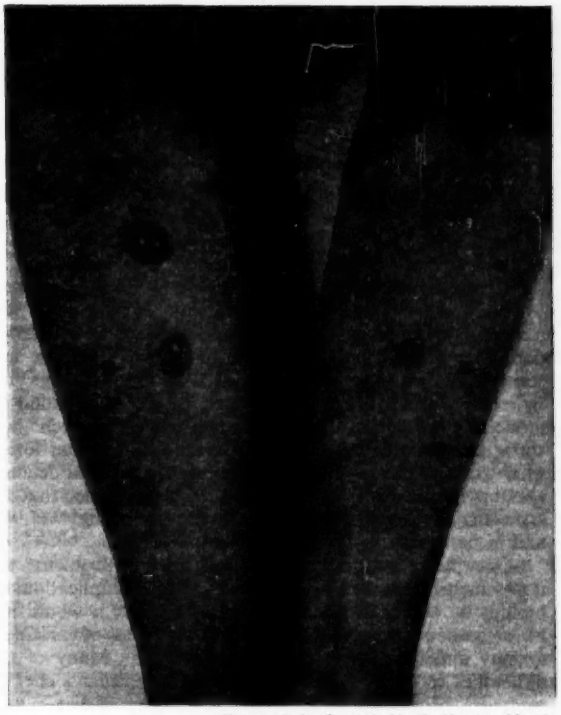
also was the action upon the eyes (Mann & Pirie, 1941)[34 38]; BAL in a strength of 5–10 % is the only compound able to save an eye when applied up to 10 minutes after contamination with an arsenical. A further "supporting" programme of work showed that, as was hoped, BAL eliminated arsenic from the skin after inunction of lewisite, with an accompanying increased excretion in the urine[61]. When injected into animals poisoned with arsenicals, it could save them even after such signs as diarrhoea had developed. The above experimental work in vitro and in vivo is excellent support for the dithiol theory.

The therapeutic applications of BAL in patients suffering from the accidents of arsenical therapy with therapeutic arsenicals, and from mercurial poisoning, are described elsewhere[l] (Thompson, 1947)[64], and are a fortunate dividend from the war-research. The exfoliative dermatitis in patients is most probably due to penetration of traces of arsenoxide (otherwise called mapharside) into the skin. Some points about this are interesting. In a brain brei, more mapharside is needed for a given degree of poisoning, and more BAL to reverse the combination[62]; similarly extra BAL is needed to treat mapharside poisoning in vivo[60]: this is interpreted to mean that mapharside-BAL is more dissociated than lewisite-BAL. With mercury there is again a difference; though BAL is more efficient, some monothiols also show some activity.

[l] [*BMB* 1199]

FIG. 5, 6. PREVENTION OF BURNS DUE TO 1 mm.-DIAMETER DROPS OF LIQUID LEWISITE ON SKIN

FIG. 5. Photo B 6415 taken at time immediately before treatment.



Photographs kindly supplied by the Ministry of Supply

FIG. 6. Photo B 6416 taken 24 hours after test.

Area	*Right Arm*	*Left Arm*
A.	Treated with antigas ointment 2 hours after contamination, when erythema was well established	Treated with BAL 10 % 2 hours after contamination
B.	No treatment (control)	No treatment (control)
C.	Treated with antigas ointment 2 minutes after application of drop of lewisite	Treated with BAL 10 % 2 minutes after application of drop

3. Further Theoretical Points

The As-dithiol compound in the tissues is slightly more dissociable than the As-BAL, and it seems certain that the ring formed with the protein was larger than one of 5 atoms. Some attempt has been made (Whittaker, 1947)[73] to throw light upon this by comparing the therapeutic efficiency in the brain-test in vitro of dithiols of constitution $HS(CH_2)_nSH$, where the number of CH_2 groups ranged from 2 to 12. The least-successful antidote was 1 : 4-butane dithiol ($SH(CH_2)_4SH$); with this, As would make a ring of 7 atoms, which in the case of other compounds has been considered by organic chemists such as Ruzicka to be a less-stable configuration. It was estimated that the stability of the As-protein in the enzyme lay between that of an eight- and a fourteen-membered ring.

The problem of the toxicity of dithiol upon injection is independently interesting and does not appear to be entirely due to the increase produced in circulating SH groups. Webb & van Heyningen (1947)[72] of Dixon's team found that BAL markedly inhibited metal-containing enzymes (cf. also Barron, Miller & Meyer, 1947)[6].

Some two years after the introduction of BAL, a fresh development took place at Cambridge. Danielli & Mitchell, who had been working in Dixon's team upon problems of permeability in relation to the war-gases, with Owen & Shaw[10 m] introduced a BAL-glucoside (BAL-Intrav). This was specifically designed for the systemic treatment of lewisite-poisoning, and to be a highly water-soluble substance, which would remain in the tissue-fluids and not penetrate cells, and would consequently be less toxic. This compound fulfils some of its promise in animals, and it is hoped that further research will make it available for clinical tests. When injected into human subjects, the glucoside increased excretion of copper and zinc in the urine (McCance & Widdowson, 1946)[32].

Little has been said about the work of others; after the initial work in Oxford and the acceptance of the value of

[m] Of the Imperial College of Science, London.

BAL at Porton, further research developed both there, in Cambridge[15] and at Edinburgh[21]. Some applications have been found in experimental arsine poisoning[19 20]. Simultaneously, the valuable researches in the USA[71] and in Canada[74] included much work upon the essential problems of the composition of ointments, the pharmacology of BAL, and other therapeutic developments.

4. General Implications

It is satisfactory that these researches carried out originally for a war-objective have repercussions in branches of science related to biochemistry. For pathology it is believed to be the first instance in which commencing damage in tissues can be reversed by a logical chemical step. We now have evidence that biochemical lesions in the oxidation stage of pyruvate can be due either to a vitamin-deficiency or to positive exposure to a toxic agent; in this sense the "enzyme" theory has grown up, though the writer would not suggest that this is the only mode of inducing cell-damage. Doubtless further research will show the importance of other enzymes along these lines; meanwhile, it can be noted that there is an especial delicacy about pyruvate oxidation, because it has been claimed that the same enzyme is also damaged in oxygen-poisoning[4 12 57 18 35] and in narcosis[51].

Some pharmacological aspects of arsenic problems are now much more clear; but, in view of the complications of biology as well as of the chemistry of arsenic, it would not be suggested that all problems in the field of arsenical toxicity and arsenotherapy are now solved[n]. Many of the difficulties to be met in the application of Ehrlich's chemoreceptor theories have been well presented earlier (Dale, 1923)[9] and are still real today; there may be mentioned as an example the selectivity of the arsenical for the protozoal tissue. Nevertheless, the application of chemistry to the cell must always be revealing when based upon a proper physiology; Ehrlich's determination (1909)[17] to apply chemistry boldly to the cell is highly stimulating, when given a modern dress; his suggestion that the arsenoreceptor might be hydroxyl (to which he gave most stress) or sulphydril (based upon Heffter) is interesting, though not based upon experiment. When Voegtlin (1925)[67] later advanced the sulphydril group as receptor, this was based upon their work with thiol substances and arsenoxide. It is a fundamental advance upon this to be able to indicate the enzyme-protein constituent attacked and the mode of attack. Short of direct evidence by isolation, it is virtually proven that the enzyme compound has an essential thiol group, and that with primary trivalent arsenicals the thiol groups are sufficiently contiguous to allow of ring formation.

During the last decade, a tribute to the inspiration of Hopkins, much work has been done upon SH enzymes[28 14 24 7] as well as upon SH groups in other proteins[66 30]; such SH enzymes require an SH group for activity. It has been learnt that such groups are not all equally activated for various inhibitors; for instance, triosephosphate dehydrogenase is much more sensitive to iodoacetate than is succinic dehydrogenase[13]. Hence there are possibilities of variation in activation as well as in spatial relation. Biochemical analysis has shown wide variations also for various trivalent arsenical compounds in the toxic inhibitions of different enzymes[23 5] and their response to thiols; many instances of reactivation by monothiols were found. Dixon[15] and his Cambridge team during the war developed the theory that vesicants attack hexokinase, the enzyme responsible for the first stage in glucose-degradation; this was based mainly upon an interesting correlation in the toxicity of various vesicants and hexokinase inhibition. To this, lewisite must be an exception; though it poisons hexokinase, the inhibition in vitro is reversed by a monothiol, whereas in vivo (as for pyruvate oxidase) a "dithiol" is necessary[o]. Presumably in cases where the toxicity of an arsenical can be reversed by a monothiol, circulating glutathione will act as a natural antidote.

During the war, independently, in Belgium, Bacq (1946, 1947)[1 2] became interested in the relation between toxicity of chemical-warfare substances and their behaviour with SH groups; lately he has introduced the term "thioloprive substances". This generalization is useful, though it will be realized that the final detail of the biochemical action will vary.

In conclusion, it is the writer's opinion that the discovery of lewisite was of real significance for this progress, because the compounds formed with it are so non-dissociable that attention was diverted from monothiols. In this sense, it is particularly appropriate to point out how closely Britain and the USA have been associated in these developments. In fact this war-research as a whole, in its course and publication, in addition to its scientific interest, has set a shining example of the excellent standards which can be reached in international co-operation.

I wish to thank Miss J. Allen for secretarial assistance, Prof. R. H. S. Thompson for reading the MS and Dr. L. A. Stocken for help with diagrams.

[n] E.g., the toxicity of diphenyl chloroarsine has still to be properly understood.

[o] The dithiol theory applies only to arsenical action; whether 2 SH groups are needed for the activity of one enzyme molecule is a different problem.

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THERAPEUTIC APPLICATIONS OF BRITISH ANTI-LEWISITE

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1 Arsenical vesicants
2 Arsenical dermatitis
a. Dermatitis due to diphenylamine chloroarsine (phenarsazine chloride)
b. Exfoliative dermatitis
c. Arsenical hyperkeratosis
3 Arsenical encephalopathy
4 Arsenical granulocytopenia
5 Mercurial poisoning
6 Gold dermatitis
7 Other metal-intoxications
References

In the production of specific antidotes against the action of toxic agents inside the animal body, one of the main objectives is to dissociate the toxic substance from the "tissue acceptor" with which it has combined, and to convert it by chemical reaction with the antidote into some stable derivative of lower toxicity, capable of excretion from the body.

As early as 1909 Ehrlich suggested on theoretical grounds that the "chemo-receptors" for arsenic in living cells might be hydroxyl or thiol groups, reaction with which would cause the metabolic disturbance characteristic of the toxic effect, and shortly after the 1914-18 war independent experimental evidence in support of this view began to accumulate (for a review of this work see Peters, 1947). Despite this knowledge, fundamental to a rational solution of the problem, no satisfactory specific therapy of arsenical intoxication had been evolved, although a number of different thiol compounds had been investigated in the hope that they might compete effectively with the tissue-thiols for the arsenic.

1. Arsenical Vesicants

At the outbreak of the recent war, however, research into the production of arsenical antidotes was actively resumed in this laboratory, chiefly in respect of lewisite and the other arsenical vesicant "gases", and by 1941 an antidote that fulfilled many of the desired theoretical criteria had been produced (Peters, Stocken & Thompson, 1945). This compound was 2 : 3-dimercaptopropanol, subsequently called British Anti-Lewisite (BAL). Until the introduction of this substance the study of potential thiol antidotes

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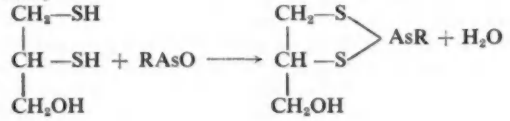
* Information available on application to Ministry of Supply, London

against arsenic had been limited to the use of monothiol compounds. Towards the end of 1940, however, Stocken & Thompson, in the course of a quantitative study of the action of lewisite on the SH-protein kerateine, isolated and analyzed the lewisite-protein compound, and showed that about 75 % of the arsenic contained in this derivative had combined in the ratio 1 As : 2 SH. This finding suggested at once the possibility that dithiol compounds might prove more effective than monothiols in antagonizing lewisite, a suggestion which was subsequently fully confirmed in animal and human experiments, no monothiol having yet been found which can prevent vesication by lewisite in man. 2 : 3-Dimercaptopropanol was synthesized and found to be the most suitable of a large number of dithiols prepared both in Britain and the USA.

This compound reacts with arsenoxides to give a five-membered-ring compound more stable than that formed between the arsenical and the " tissue-acceptor ", and very much more stable than the compound formed between arsenicals and monothiols (Stocken & Thompson, 1946a, 1946b).



BAL is a colourless oil, approximately 6 % soluble in water at room-temperature ; it is stable in the pure state, or when dissolved in non-aqueous media, but is rapidly oxidized in aqueous solution near the neutral point. Laboratory animals contaminated or injected with lethal amounts of lewisite can be effectively treated by the use of BAL applied either on the skin or by injection, a significant increase in the urinary excretion of arsenic resulting (Stocken & Thompson, 1946c). The blistering effect of lewisite on human skin can be prevented by the local application of BAL to the affected area as late as 1½ hours after contamination. This fact in itself provides evidence of the ability of BAL to *reverse* the toxic action of lewisite, since its application to the contaminated area can be delayed until after intense erythema has appeared ; instead of progressing to the usual tense vesicle overlying an area of necrosis, the erythema in most cases disappears almost completely within 24 hours of the treatment.

Apart from these experimental results, BAL was used successfully during the war years for the treatment of accidental splashes of arsenical vesicants on the skin of factory-workers. Cases of accidental contamination of human eyes with arsenical vesicants were fortunately few, but the reports received indicated that those treated with BAL supported the general results of animal experiments, in which it had been found that the instillation into the conjunctival sac of a 5 % or 10 % solution of BAL within 5 minutes of contamination resulted in almost complete recovery.

The importance of determining the efficacy of BAL against the toxic effects of the therapeutic arsenicals was early realized, and in 1942 work was begun with this end in view both in Britain and the USA. In Oxford, Stocken, Thompson & Whittaker (1947) showed that BAL can protect the pyruvate-oxidase enzyme-system of brain against mapharside, neoarsphenamine and arsphenamine, and is also effective in maintaining the survival of rats after the injection of lethal doses of mapharside or neoarsphenamine. In America, Eagle in 1943 demonstrated that BAL can resuscitate micro-organisms poisoned by mapharside, and is also of value in the treatment of acute or subacute mapharside poisoning in rabbits (Eagle, Magnuson & Fleischman, 1946) ; in the course of this work these investigators found that solutions of BAL in arachis oil containing benzyl benzoate could be sterilized by heat with only slight loss in activity.

Before this finding, work had been started on the treatment of arsenical dermatitis in man by the inunction of BAL ointments (Longcope, Luetscher, Wintrobe & Jager, 1946 ; Carleton, Peters, Stocken, Thompson, Williams, Storey, Levvy & Chance, 1946), but although distinctly encouraging results had been obtained, the irritant action of BAL on human skin, more pronounced on skin already inflamed, indicated that inunction was not an entirely satisfactory method of administration. Eagle's finding therefore was an important advance, since ampoules of the compound suitable for intramuscular injection into man could be readily prepared. In Britain, the ampoules finally used, prepared by a modification of Eagle's method, contained 5 % BAL in arachis oil and benzyl benzoate, the ampoules being nitrogen-filled and sterilized by heating for 1 hour at 170°C.

The treatment of a number of different metal-intoxications with BAL has now been investigated, and will be considered under the following headings.

2. Arsenical Dermatitis

a. Dermatitis due to diphenylamine chloroarsine (phenarsazine chloride)

The first application of BAL to the treatment of widespread arsenical lesions in man was carried out by Longcope, Luetscher, Wintrobe & Jager (1946) in 7 cases of dermatitis occurring in workers exposed to the dust of diphenylamine chloroarsine (also known as DM). The lesions involved the exposed areas of the face, neck and arms, and had proved intractable to the standard forms of treatment, having been present, in 6 of the patients, for from 18 to 50 days before admission to hospital. Treatment with daily applications of BAL ointment caused the dermatitis to clear completely in from 2 to 8 days, with an average of a little over 5 days. In the course of this work it was shown that successful results could be obtained by inunction of the ointment into areas of normal skin, the BAL, after absorption, bringing about detoxication in the affected areas ; by this means it was possible to avoid the intense burning sensation produced by the application of BAL to erythematous skin.

b. Exfoliative dermatitis

Considerable experience has now been accumulated in the treatment of exfoliative dermatitis occurring as a complication of arsenotherapy. In a first series of 30 patients Carleton *et al.* (1946) have reported a beneficial effect in approximately 50 % of cases ; 21 of these were treated by intramuscular injection, and the remainder by inunction.

In a more recent report (Carleton, Peters & Thompson, 1948) the results obtained in a further 44 cases have been described. Of these cases 41 were of the acute exfoliative type, and the dermatitis was in all cases severe and wide-

spread. The BAL was given by deep intramuscular injection into the gluteal region, the following course of injections being given in most cases :

First day : 4 injections of 2 ml. 5 % BAL at 4-hourly intervals ;
2nd, 3rd and 4th days : 2 ml. twice daily ;
5th and 6th days : 2 ml. daily.

From the reports received from the clinicians who co-operated in this trial, it has been concluded that a " good " response was obtained in 23 cases (52 %), while if 8 further cases in which a " fair " response was obtained are included, the number of those benefited by the treatment is 31 (70 %). In some cases an almost dramatic response was obtained, and the mean duration from the first injection of BAL to healing or nearly complete healing was 21 days. Photographs of one of the cases described in that report are given in fig. 1 and 2.

In America, Longcope *et al.* (1946) have described 15 cases of generalized exfoliative dermatitis following the use of anti-syphilitic arsenical drugs, and have stated that symptomatic and objective improvement regularly followed the administration of BAL. Luetscher, Eagle, Longcope & Watson (1946) have, in addition, followed the arsenical excretion in 16 cases and have shown that, in a proportion, BAL-therapy causes an increased elimination of arsenic in the urine. Carleton *et al.* (1946) also studied the urinary arsenic-level in a number of cases, but were unable to detect any significant increase following treatment with BAL. The absolute amounts of arsenic appearing in the urine are, however, small, and owing to the variations in the day-to-day excretion and to the long intervals which in some cases elapsed between the last injection of arsenic and the beginning of treatment, this result is not surprising.

The american workers, however, have used 10 % solutions of BAL and in severe cases have given a higher dosage than that used in Britain.

In several instances, clinical evidence of relapse has been obtained shortly after the end of BAL therapy. This has in every case responded satisfactorily to a further short course of injections.

c. Arsenical hyperkeratosis

An account of one case of arsenical hyperkeratosis of the palms and soles, together with marked pigmentation of the lower trunk and thighs, has also been received. This patient was given 2 courses of BAL therapy at an interval of a month. It was concluded that a definite reduction of the keratosis occurred in response to the treatment, accompanied by an almost complete disappearance of pigmentation. Although this is the only report of such a case, it is of interest in view of the chronic nature of this type of lesion.

3. Arsenical Encephalopathy

In a report of the Council on Pharmacy and Chemistry of the American Medical Association (1946) a brief account is given of the use of BAL in the treatment of 55 cases of " haemorrhagic encephalitis " caused by intensive arsenotherapy. Eleven deaths occurred in this series, but the remaining 44 patients recovered completely in 1 to 7 days. In 5 of the 11 fatal cases BAL was not injected until from 9 to 72 hours after the onset of convulsions or coma.

In Britain, BAL has been given in 3 cases. In 2 of these complete recovery took place in less than 1 week, while in the third, consciousness was recovered on the fourth day and an uninterrupted recovery with no residual sequelae followed.

4. Arsenical Granulocytopenia

Although the number of cases so far studied is small, BAL also appears to be of value in the treatment of granulocytopenia occurring during arsenotherapy. A favourable response in the leucocyte-count, with a proportionately greater increase in the number of polymorphonuclear leucocytes, occurred in 10 of 11 cases reported in the USA (Council on Pharmacy and Chemistry, 1946). Five cases have also been treated with BAL in Britain ; in each case a rapid restoration of the leucocyte-count occurred.

5. Mercurial Poisoning

Preliminary work on enzyme-systems and on laboratory-animals (Gilman, Allen, Philips & St. John, 1946 ; Thompson & Whittaker, 1947 ; Stocken, 1947) has shown that BAL can also detoxicate mercury. An interesting series of 23 cases of acute poisoning by mercuric chloride in man, treated with intramuscular injections of BAL, has been described by Longcope & Luetscher (1946). The amounts of mercury swallowed by these patients varied from 0.5 to 20 g. of mercuric chloride. 22 of the 23 patients recovered completely, the one death being in a patient who was not treated with BAL until 13 hours after taking the mercury.

6. Gold Dermatitis

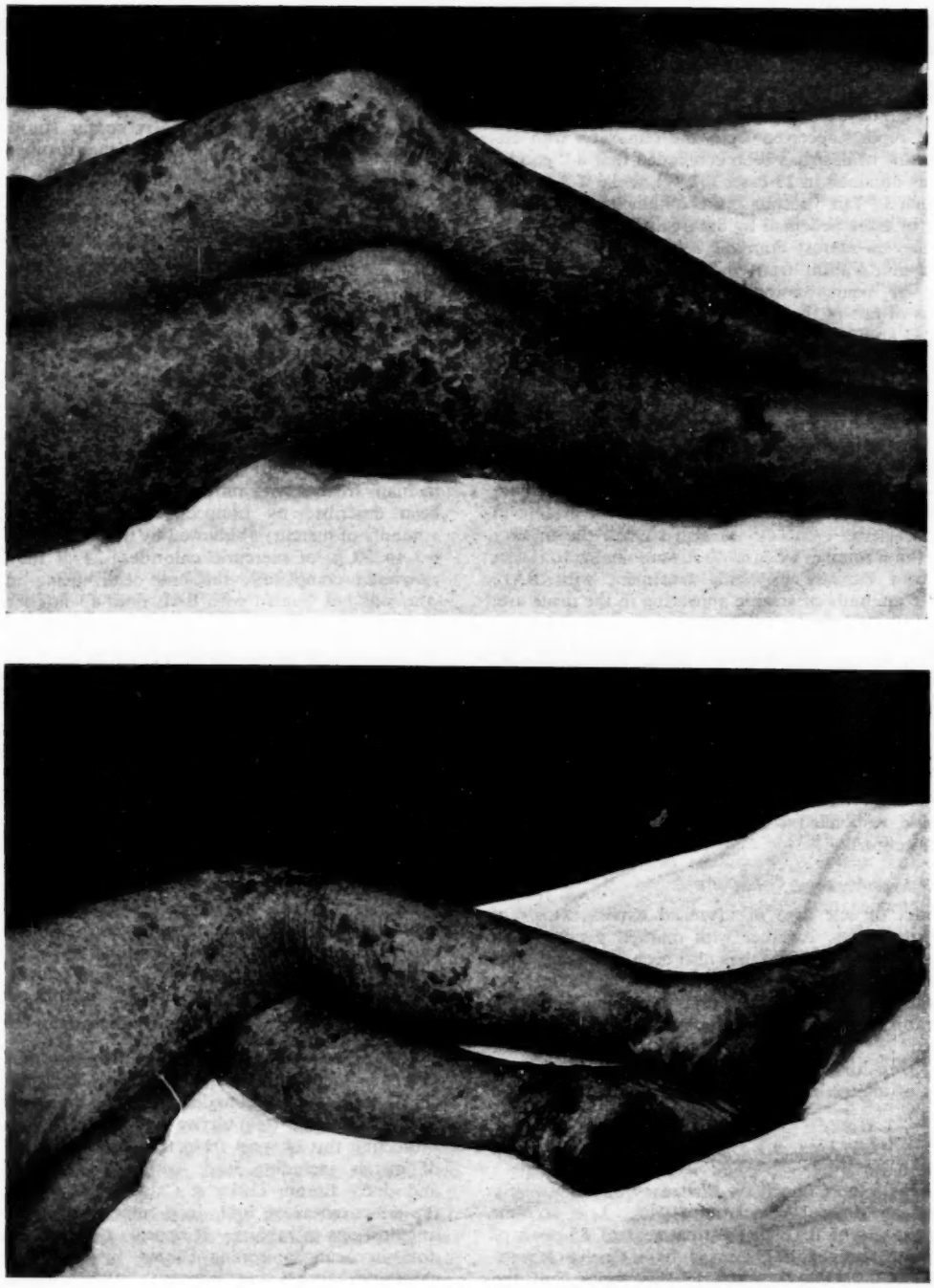
In 1945, experiments with the pyruvate-oxidase system of brain (Thompson & Whittaker, 1947) indicated that BAL might be of value in the therapy of gold-intoxication, and clinical reports have now appeared supporting this view. Cohen, Goldman & Dubbs (1947) and Ragan & Boots (1947) have described beneficial effects in the treatment of gold dermatitis, and the latter workers have also claimed that a significant increase in the excretion of gold in the urine accompanied the treatment. A few cases have also been studied in Britain with encouraging results.

Lockie, Norcross & George (1947) have also reported a case of thrombocytopenic purpura and another of granulocytopenia due to gold, both of which responded promptly to treatment with BAL.

7. Other Metal-Intoxications

Studies of therapeutic possibilities in connexion with other metals are still in an early stage. Barron & Kalnitsky (1947), using the succinoxidase enzyme-system, have shown that BAL and certain derivatives of BAL are effective in protecting this enzyme from the toxic effects of a number of metals including lead, antimony, bismuth, cadmium and zinc. Braun, Lusky & Calvery (1946) have examined the effectiveness of BAL in a number of different metal-intoxications in rabbits. It appears to be an effective antidote in acute poisoning caused by antimony, bismuth, chromium, nickel and mercury, but is ineffective against lead, thallium and selenium ; in the case of lead and selenium, indeed, BAL appeared to produce an additive toxicity. Its use in experimental cadmium-poisoning has

FIG. I. ARSENICAL DERMATITIS BEFORE TREATMENT



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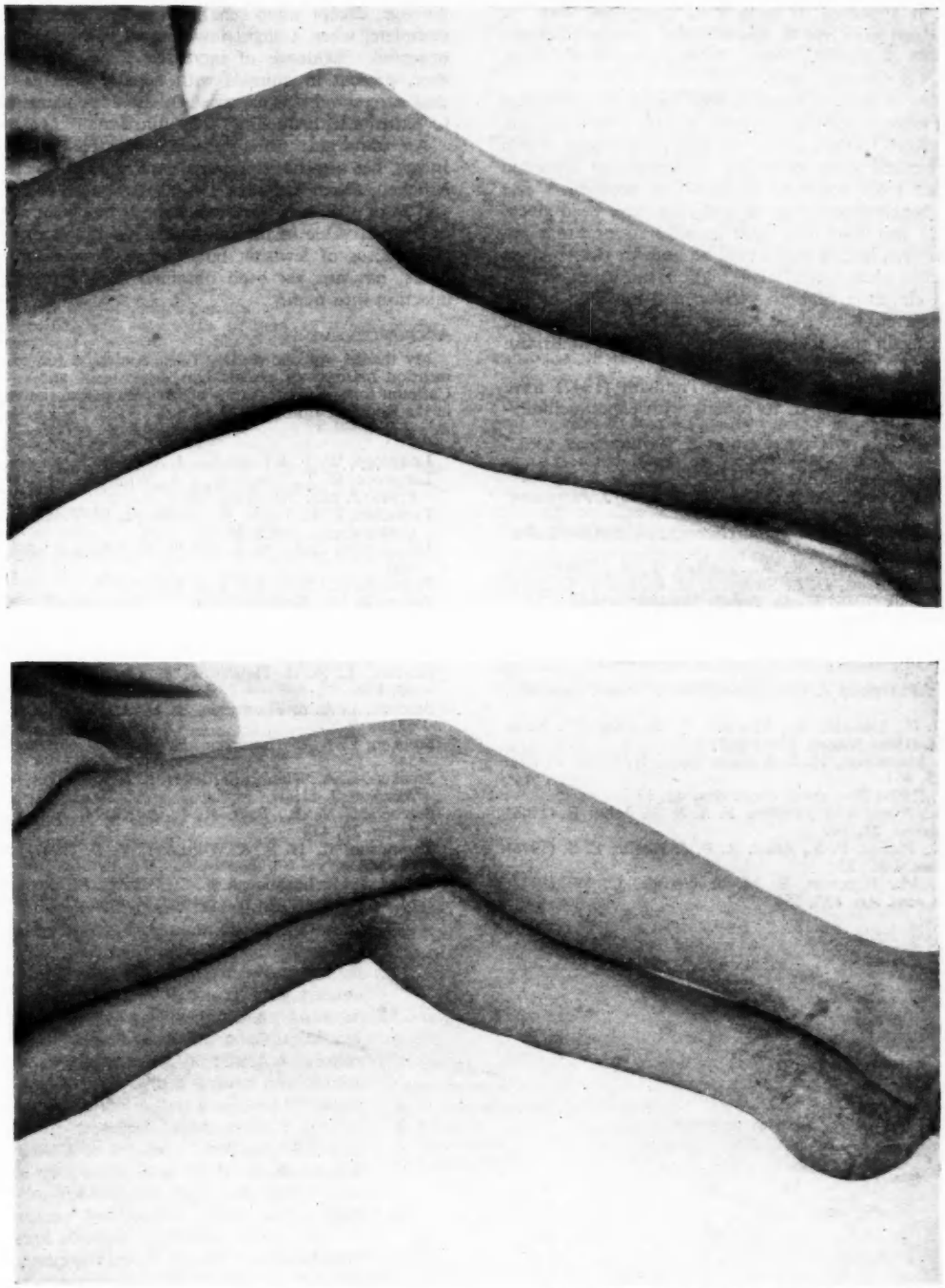
The photographs show the condition on the day (14/6/46) of commencement of treatment with BAL

FIG. 2. ARSENICAL DERMATITIS AFTER TREATMENT WITH BAL



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The photographs show the same case as in fig. 1, 14 days later

been studied extensively, but although it has proved of value in protecting animals from the systemic effects of this metal, it appeared to form toxic complexes with the cadmium which gave rise to serious renal damage (Gilman, Philips, Allen & Koelle, 1946; Tobias, Lushbaugh, Patt, Postel, Swift & Gerard, 1946).

The toxicity of BAL to man has been the subject of careful study in America (Sulzberger, Baer & Kanof, 1946; Modell, Gold & McKeen Cattell, 1946). In brief, it has been shown that the minimal dose given by intramuscular injection which causes toxic reactions in man lies between 3 and 5 mg./kg. Single doses of up to 8 mg./kg. have been given, and even at this level the toxic manifestations are completely reversible, lasting only about an hour or two. Apart from subjective phenomena, lachrymation, salivation, vomiting and an elevation of both systolic and diastolic blood-pressure occurred with these higher doses. It should be pointed out again that the therapeutic dose used in Britain is only about 1.5 mg./kg. bodyweight.

In Britain, Cameron, Burgess & Trenwith (1947) have studied the toxicity of BAL to rabbits with experimentally-induced renal and hepatic damage. No evidence was obtained of any increased toxicity in animals with renal damage, except when renal failure was complete or nearly complete, when a slight lowering of tolerance to BAL was observed. Evidence of increased toxic effects was, however, present in animals with hepatic damage, suggesting that care should be exercised in the administration of BAL to patients with impaired liver-function.

An important water-soluble derivative of BAL, BAL-Intrav, has also been prepared in Britain (Danielli, Danielli, Mitchell, Owen & Shaw, 1946). It is a glucoside of BAL, and is of strikingly low toxicity. It has been shown to be of distinct value in the treatment of animals poisoned with large doses of lewisite, but, except for experimental purposes, has not yet been obtained in a form suitable for injection into man.

ACKNOWLEDGEMENTS

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HUMAN BIOCHEMICAL GENETICS

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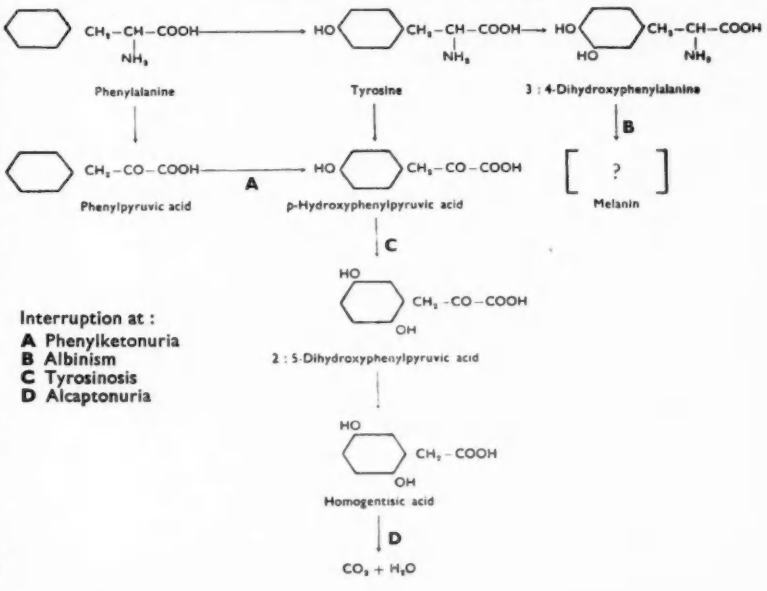
1 Methods of biochemical genetics
2 Difficulties and advantages of man as a subject for chemical genetics
3 Prospects of human chemical genetics
4 Non-genetic heredity
5 Future progress
References

The study of biochemical reactions influenced in vivo by genes, or conversely the study of genes that control biochemical processes in vivo, is the subject-matter of biochemical genetics. Since the general acceptance of Mendel's principles after their rediscovery in 1900, it has seemed likely that many genes exert their influence by affecting the course of chemical reactions in the organism. This influence may be direct or indirect. The primary action of a particular gene may be concerned, for example, with the synthesis of a coenzyme. A mutation of this gene to an inactive form, followed by the production of an organism homozygous for it, would result in an organism in which a number of reactions dependent on coenzyme would now be impossible and in the organism being viable only in the presence of external sources of coenzyme. Thus, it might appear that mutation of a single gene was responsible for the failure of several reactions (secondary effects), though the immediate effect is the failure of one reaction only (primary effect). It may be argued that the chain of events could be followed further back—that the mutation might be responsible for failure to synthesize not a coenzyme, but an enzyme responsible for coenzyme-synthesis, or even an enzyme-precursor of the enzyme responsible for coenzyme-synthesis. At present, however, it can be said that some genes have definite effects, among which can sometimes be found a primary effect that is connected with a definite biochemical reaction. The hypothesis that genes act by means of their control of biochemical reactions, that there is a "one gene, one reaction" relation, and that where a gene appears to have other effects (such as psychical or morphological) these will be found to be consequent on biochemical effects, seems likely to be a fruitful stimulus to further work.

The first demonstration that such gene-controlled reactions occur was made by Garrod in his pioneering work *Inborn errors of metabolism* (1909). Garrod discussed fully the biochemical and genetic aspects of alcaptonuria and laid the foundations of the study of biochemical genetics. In 1914, Gross discovered an enzyme present in the serum of normal individuals, and absent from the sera of alcaptonurics, capable of catalyzing the oxidation of homo-gentisic acid. This enabled Garrod, in the second edition of his book in 1923, to complete the demonstration that alcaptonuria was due to the absence of a gene responsible for producing an enzyme catalyzing a relatively-simple biochemical reaction; but his work was almost completely ignored by geneticists until its significance was emphasized in recent years, notably by Haldane.

Since that time, only one other chemical reaction controlled genetically, in which *both initial and final products* of the reaction are of known composition, has been discovered in man. In this, the absence or inactivity of the gene results in the appearance of phenylpyruvic acid in the urine. This condition, discovered by Følling in 1934, was subsequently thoroughly investigated in Britain by Penrose (Penrose, 1935; Penrose & Quastel, 1937). Like alcaptonuria, the condition is inherited as a recessive character, and appears to be due to the absence in affected subjects of a gene controlling, in some way, the ability to oxidize phenylpyruvic acid to *p*-hydroxyphenylpyruvic acid. A single case of a related biochemical disability has been noted in a subject unable to oxidize the latter compound to the 2 : 5-dihydroxy compound (Medes, 1932). Since only one case has been studied, it has not been possible to show that this condition, too, is inherited as a recessive, though there is every reason to believe that it is. A summary of these genically-controlled disabilities in the oxidation of phenylalanine and related compounds is reproduced as fig. 1 (after Haldane, 1941). Other hereditable peculiarities of metabolism in man that appear likely to have a relatively-simple

FIG. 1. PHENYLALANINE-TYROSINE METABOLISM IN MAN (BASED ON HALDANE, 1941)



biochemical cause of the type responsible for alcaptonuria and phenylketonuria, are congenital steatorrhoea, pentosuria, cystinuria and haematoporphyria.

Hair- and skin-colour in man is due to the presence or absence of melanins. The melanins are complex substances whose composition is obscure, and their study is made more difficult by the facts that they are insoluble and the degree of physical dispersion may cause variations in their colour, though not necessarily in their composition. The inheritance of coat-colour in the guinea-pig has been intensively studied by Wright (1941), who has shown that at least seven genes are involved, some of which are concerned with pigment-synthesis and some with follicle-differentiation. Non-genic agents may also be involved (Billingham & Medawar, 1947). Owing to the number of genes involved, and the complex nature of their end-products and interactions, it seems unlikely that an understanding of the inheritance of pigmentation, and the characterization of the reactions involved, will soon be achieved for man.

1. Methods of Biochemical Genetics

Until recently, biochemical genetics has been concerned with defects of metabolism that are not usually of prime importance to the organism. That this is so, follows from the fact that only those defects are open to observation which are not sufficiently serious to kill the subject before its metabolism can be examined. A further limitation is imposed by the fact that the vast majority of mutations are recessive, and are therefore usually masked by the presence of a dominant allele whose influence can be eliminated only by breeding-experiments. Much fruitful recent work has been rendered possible by avoiding this difficulty by the use of organisms that can be investigated in the haploid stage. Among such organisms are some yeasts and moulds, *Saccharomyces* and *Neurospora* in particular. These organisms have the further advantage that the generation-time is short—6 days for *Saccharomyces*. The advantage of a short generation-time was of course realized early, and accounts largely for the intensive use of the fruit-fly Drosophila (generation 10 days) in genetical studies. Although bacteria, which have a short generation-time and are well suited to biochemical study, undergo changes apparently similar to mutation in higher organisms, they are not susceptible to genetical study as their reproduction is vegetative.

Although genically-controlled biochemical disabilities which would be lethal to the organism cannot be studied in most subjects, *Neurospora* has been used in this way (Beadle, 1945a). *Neurospora* is a mould that will normally grow well on a very simple medium containing only salts (including a nitrogen-source), an energy-source, such as a suitable fat or carbohydrate, and the vitamin biotin. Irradiation of *Neurospora* peritheca prior to reduction-division results in the production of ascospores which may contain mutant genes. On germination, these ascospores form a haploid mycelium which should show the effect of any mutations produced. Some of these mutations will be such that the organism is no longer able to synthesize all the compounds normally required in its metabolism. Such a spore would not therefore be capable of growth on a simple medium, and the mutation could be classed as lethal. If, however, the spores are allowed to germinate on a medium containing as many substances, likely to be of importance in the mould's metabolism, as the investigator can supply, growth may occur. If transfer to the simple medium shows that such a mutation has occurred, the use of the medium supplemented singly with known compounds will reveal the particular failure in synthetic ability that has been induced. An examination of the mutants obtained in this way has added a great deal to our knowledge of chemical genetics. It has been shown, for example, that no less than 7 genes are concerned in the synthesis of the amino-acid arginine by *Neurospora* (Srb & Horowitz, 1944). Further analysis of these mutants has rendered it likely that each of these genes is concerned with a single stage of the synthesis (fig. 2).

FIG. 2. ARGININE SYNTHESIS IN NEUROSPORA

Genes controlling steps in this scheme are identified by the numbers of the mutant strains in which they were first found (Srb & Horowitz, 1944).

Strain 21502, 27947, 29997, 34105 → Ornithine → Citrulline → Arginine (Strain 33442, 30300; Strain 36703)

NOTE: That two reactions were concerned in the transformation of ornithine to citrulline was suggested by Srb & Horowitz because two genes were necessary. It had been suggested earlier by Krebs (1936) that two reactions were likely to be involved:

$$\underset{\text{ornithine}}{R \cdot CH_3(NH_2)} + CO_2 \rightarrow \underset{\text{δ—carbamino ornithine}}{R \cdot CH_2NH \cdot COOH}$$

and

$$\underset{\text{δ-carbamino ornithine}}{R \cdot CH_2NH \cdot COOH} + NH_2 \rightarrow \underset{\text{citrulline}}{R \cdot CH_2NH \cdot CONH_2}$$

Work on the biochemical genetics of *Saccharomyces* is of considerable theoretical importance, in that it has shown that changes in a gene may be obscured by cytoplasmic effects. A diploid yeast, heterozygous for the gene controlling the formation of an enzyme responsible for ability to ferment the sugar melibiose, will produce under normal circumstances four haploid ascospores of which only two will be capable of melibiose-fermentation on germination, owing to the segregation of the gene responsible. If, however, melibiose is present throughout copulation and ascospore-formation, the cultures derived from the four ascospores will all be able to ferment melibiose. Segregation of the gene responsible has occurred in the normal manner, however, for it can be shown that two of the cultures will lose permanently the ability to ferment melibiose if grown in its absence, while the other two do not. Thus, it must be concluded that the enzyme responsible, or a precursor, is capable of self-reproduction as long as its substrate is present. It is possible that, if this mechanism is shown to be of wide occurrence, it may prove that some enzymes acting on substrates invariably present in cells may no longer be produced under genic control, but may be perpetuated by a cytoplasmic mechanism.

As a result of work on haploid organism, no less than 9 of the total 25 genically-controlled reactions listed in the recent review by Beadle (1945b) have been discovered, and another 4 are accounted for by the work of Moewus on sex phenomena in *Chlamydomonas*. Thus, rather more than half the data of chemical genetics derives from the study of micro-organisms.

After micro-organisms, the most fruitful type of material quantitatively has been the higher plants, which account for a further seven reactions. These include those responsible for anthocyanin synthesis, glucoside hydrolysis, and a carotinoid transformation, and are not of great interest for the present purpose, though adding to the evidence that each step in a synthesis may be controlled by a single gene. A reaction involving an oxidation of tryptophan in insects, the hydrolysis of atropine in the rabbit, and the formation of allantoin from uric acid in dogs, completes the list of known reactions, with the addition of the two already described for man.

A consideration of the results so far described gives reason to believe that many of the metabolic processes of man will be found to be under genic control. The accumulation of knowledge related to metabolism in man may enable some conditions, found to be due to abnormal metabolism, to be controlled by supplying substances that cannot be synthesized, or by excluding from the diet substances whose abnormal metabolism may lead to disease. It may be argued that vitamin therapy is an example of this method, for there is no sharp distinction between the treatment of a *Neurospora*-mutant incapable of synthesizing thiamin, by supplying it in the culture-medium, and treating scurvy in man by ascorbic acid, which other mammals can synthesize, though man cannot.

2. Difficulties and Advantages of Man as a Subject for Chemical Genetics

The difficulties inherent in the study of the genetics of man have been summarized by Crew (1946), who points out that a

> species which lives in an environment created by itself, and which is notable for its variety, must present considerable difficulties when the species itself reproduces so slowly, has so few offspring, fails to maintain pedigrees, and cannot be used as experimental material.

There are, however, advantages in the study of man. The population available for study is large, and the presence of abnormality of any kind in a large part of it is likely to be brought to the attention of medical men and through them to that of geneticists. The study of human genetics also widens the range of data available, since the subject can describe reactions to stimuli that would otherwise be hard to determine. It is a simple matter to examine human beings for colour-blindness, more difficult and time-consuming for bees or birds. The study of mental symptoms which may occur as end-effects of simple failures of metabolism (imbecility in phenylketonuria) is not only of great practical importance but almost impossible in other experimental material.

3. Prospects of Human Chemical Genetics

The possible applications of a fuller knowledge of biochemical genetics of man may be divided into :

i. Avoidance of the full expression of deleterious genes.

ii. Avoidance of deleterious consequences of gene-action.

iii. The suppression of undesirable genes.

Many genes give rise, not to the invariable manifestation of a character, but to a predisposition to a character that may be exhibited only after some stimulus, presumably environmental in origin. The absence of sweat-glands, for example, may not be noticed in the british climate, but transfer to the tropics makes it obvious. In other examples, the exciting factor that may cause the exhibition of symptoms of conditions hitherto latent is not known. Epileptics show a characteristic wave-pattern in electro-encephalograms, and similar patterns occur in non-epileptic subjects who may be supposed to have inherited epileptic tendencies. Only about one in twenty of subjects with the epileptiform electroencephalogram is an epileptic, and present evidence indicates that the predisposition is inherited as a simple Mendelian dominant (Lennox, Gibbs & Gibbs, 1939). Further research may succeed in identifying the evocative conditions, and enable them to be avoided by those disposed to epilepsy.

Even if the action of a gene cannot be avoided, its ill effects may be circumvented. The occurrence of blood-group antigens is genically-controlled in man, and among them the rhesus series is of importance in the study of haemolytic disease of the newborn (Race, 1946).[1] While no example is known of antibodies to rhesus antigens occurring spontaneously, they are readily formed in response to immunization. This immunization may be due either to transfusion of blood containing rhesus antigens not present in the recipient's blood, or to the introduction of such antigens from the foetus into the circulation of the mother. The maternal rhesus antibodies formed in response to this iso-immunization may travel across the placenta, causing haemolysis in the foetus. Haemolytic disease of the newborn in those cases (the majority) due to the rhesus incompatability between mother and child is, of course, determined genically, since the occurrence of the antigens responsible is genically determined. It is, however, another example of a condition that is shown in only a small number of the cases in which it might be expected. About one pregnancy in ten is such that the necessary antigen-distribution between mother and child is present, yet evidence of maternal antibody-formation is obtained in only about one in 250 pregnancies. It has been shown that some of those cases of haemolytic disease of the newborn not explicable on the basis of rhesus incompatability may be due to incompatability of the ABO groups—a condition hitherto unnoticed owing to the great rarity of the response in conditions apparently favourable (Aubert, Cochrane & Ellis, 1945).

When haemolytic disease of the newborn does occur, it may vary in severity. Effects range from jaundice to kernicterus and hydrops foetalis. When the effects are limited to jaundice, cure is possible by transfusion of blood not haemolyzed by the antibodies present in the infant's plasma. Haemolytic disease of the newborn is thus a good example of a genically-controlled disease in which the primary gene-effect (antigen-formation) is intrinsically harmless but may lead to secondary effects of a varied and severe nature. It is also a genically-controlled disease that can be successfully treated in some cases. It is possible that, when the chemical structure of the hapten portion of the blood-group antigens is known, they may be synthesized and used in the treatment of the disease in utero, for it

[1] [*BMB* 872]

might be possible by their use to keep the maternal antibody-level low enough to avoid significant transfer across the placenta.

The complete suppression of undesirable genes may be attempted in two ways. The first is that of controlled breeding, or eugenics, and will not be discussed. The second is selective mutation. Agents are known that may be used to increase the mutation-rate, but none is selective; they may be said to lead to increase in the spontaneous mutation-rate of all genes. Among these are a number of chemical compounds, one of which, allyl*iso*thiocyanate, occurs naturally in some plants (Auerbach & Robson, 1944). Other far more effective compounds are mustard-gas and some related compounds (Auerbach & Robson, 1946). Mustard-gas is a very powerful agent indeed, giving as high a mutation-rate as *x*-rays. These agents are non-specific, but it is possible that the investigation of the nitrogen- and sulphur-mustard groups which already show some *tissue* selectivity (Gilman & Philips, 1946) may lead to the discovery of compounds with some selective action on mutation. The demonstration by Demerec (1947) that the carcinogen 1 : 2 : 5 : 6-dibenzanthracene is also mutagenic will lead to the investigation of some of the large number of known carcinogens, and the relation between carcinogenic and mutagenic power in these should prove to be of the greatest interest.

The possibility of inducing mutation in a particular gene has led to some experimental work that is unfortunately inconclusive at present. In 1920 Guyer & Smith claimed that they had induced heritable eye-defects in rabbits by the injection of antisera against eye-lens protein into pregnant rabbits. Attempts were made by other workers to confirm these results but were unsuccessful. Recently, however, Sturtevant (1944) has said that Hyde succeeded in confirming the work of Guyer & Smith just before his death in 1943. Sturtevant's interpretation of this finding is that there is a similarity in molecular shape of the gene and the antigen it produces. Thus, antibody may combine with the gene and interfere with its duplication in such a way that the genes produced are not effective in antigen-production. This is tantamount to the induction of specific mutation. Emerson (1944) attempted to induce similar mutations in *Neurospora* by treatment with antisera prepared against *Neurospora* mycelium or *Neurospora* culture-filtrates. The material used was a mixture of antigens, and presumably gave a very varied collection of antibodies. It was found that the mutation-rate of *Neurospora* was increased by antibody treatment, but this may well have been a non-specific effect, for no controls with normal sera were done and owing to the probably-mixed nature of the antibody used, specific effects would not have been easy to detect. In spite of the interest of this work it has not been repeated or confirmed. There seem to be a number of probable difficulties in bringing gene and antibody into contact, for it is necessary not only to move antibody across the cell-membrane but to maintain a sufficient concentration of it once there, in the presence of intracellular proteases that are likely to break up foreign proteins. It seems unlikely that such methods of specific mutation will become of practical interest in human genetics, more especially because they are likely to inactivate genes, rather than restore genes that have lost their function, and consequently are likely to be of value only in modifying dominant genes.

4. Non-genetic Heredity

At present there is great interest in types of inheritance that involve cytoplasmic factors for which the name "plasmagenes" has been coined. It is supposed that, like genes, these are capable of self-duplication, and that they may have properties such as to constitute a link between virus and gene. In addition to the very considerable body of speculation on cytoplasmic inheritance, there is some definite evidence that it does occur. In plants, the plastids are known to be self-duplicating bodies, liable to sudden changes that are then perpetuated. Their duplications seems to be influenced to some extent by genes. The work of Lindegren (1945) on cytoplasmic inheritance of a sugar-splitting enzyme in *Saccharomyces* has already been discussed; other work emphasizing the close interrelations that exist betweeen intra- and extra-nuclear inheritance is that of Sonneborn (1945) on the "killer" character of *Paramecium*. The demonstration that one of the factors responsible for mammary cancer in mice appears to be extra-nuclear and self-duplicating may lead to work on cytoplasmic inheritance in higher animals. This field is discussed more fully by Haddow (1947)[1]. It had long been apparent that many of the factors responsible for the production of an adult from a fertilized egg were cytoplasmic. All cells in the body have the same genic constitution, but they differ greatly from each other. That this difference is not merely one of environment is demonstrated by tissue-culture in which cells do not all revert to the same type, in spite of having the same environment. In tissue-cultures, at least four distinct types of cell which all have the same genic constitution are recognizable. It may be concluded then, that these differences are due to self-duplicating cytoplasmic factors. Studies of inheritance in bacteria and mutation-like changes in viruses, such as phage, may be relevant to cytoplasmic inheritance in higher organisms.

5. Future Progress

Biochemical genetics is hampered at present by our lack of knowledge of the structure of most of the more-important constituents of the cell. It is commonly assumed that the genes are nucleoprotein in nature, but we know little of the fine structure of proteins and less of the structure of nucleic acids. One of the plant-viruses was shown to contain nucleic acid in 1936 (Bawden, Pirie, Bernal & Fankuchen), yet it was not until 1947 that it was shown that this nucleic acid had 3 mononucleotides of the same composition as 3 of the 4 mononucleotides of nucleic acid from yeast (Schwerdt & Loring, 1947). About the order in which the components of nucleic acids are arranged, nothing is known, though there is evidence from the extremely fine specificity of the type-determining nucleic acids responsible for pneumococcal-capsule synthesis, that order and arrangement in space of the components may be of the greatest importance in determining specificity. The work of Todd and his school in Britain gives ground for hope that the synthesis of simple nucleic acids is not very far off (Todd, 1946). In our knowledge of the structure of the proteins we are more advanced, but again little is known of the order of different amino-acids that make proteins. A third class of high-molecular-weight polymers is the polysaccharides.

[1] [*BMB* 964]

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DEVELOPMENT OF IDEAS ON THE NATURE OF VIRUSES

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1 Size as a criterion
2 The physico-chemical approach
3 Microbes or molecules?
4 Nature of the fundamental virus-particles
5 Combination of virus with tissue-constituents
6 Conclusions
References

The idea that a disease can be contagious, that is, caused by direct or indirect contact with another case of the disease, is old. It appears in the Old Testament and the Decameron, to cite popular writing as evidence of a more or less general acceptance, and it was set out in a manner acceptable to scientists by Fracastorius (1546). Until bacteria had been recognized by the early microscopists no suggestions, based on evidence, were made about the nature of the infective agents. During this period the word virus was used indiscriminately to cover agents, such as snake-venoms, which cause pathological states that are not transmissible from one victim to another, and also infective agents. The restriction of the word to infective agents came with Pasteur's unequivocal demonstration of the role of bacteria in causing disease, and it was then used for any infective material, whether an organism had been recognized in it or not. As an example of this broad use Pasteur may be quoted (1889); the translation by Ruffer is used because it appeared a year earlier than the french version of this article.

> Moreover, it is not difficult to prove that rabies is a disease which cannot appear *de novo* under any physiological conditions, and that its spontaneous origin is quite impossible. We know nowadays that contagion or virulent affections are caused by small microscopic beings which are called microbes. The anthrax of cattle, malignant pustule of man, is produced by a microbe; croup is produced by a microbe . . . The microbe of rabies has not been isolated as yet, but judging by analogy, we must believe in its existence. To resume: every virus is a microbe. Although these beings are of infinite smallness, the conditions of their life and propagation are subject to the same general laws which regulate the birth and multiplication of the higher animal and vegetable beings.

On the strength of this and some other passages the suggestion that the agents causing certain diseases could be smaller than the visible bacteria is sometimes attributed to Pasteur. It is clear however that he wisely refrained from making any suggestion to explain his inability to find a rabies organism.

Ivanowski (1892) found that the sap from plants suffering from tobacco mosaic retained its infectivity after passage through a Chamberlain filter-candle but, being convinced that the disease was due to a bacterial infection, he argued that the symptoms might be due to bacteria penetrating the candle or to a toxin secreted by the bacteria. He could have disproved the latter suggestion by demonstrating that plants which showed symptoms as a result of inoculation with the filtrate had an infective sap, but he does not appear to have done so. This experiment was carried out with foot-and-mouth disease by Loeffler & Frosch (1898). They tried to make a vaccine by removing the infective particles from vesicle-lymph by passage through a filter-candle, but

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HUMAN BIOCHEMICAL GENETICS

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Many antigens owe their specificity to the polysaccharide moiety of the whole, among them those of the blood-groups and those responsible for type-specificity of pneumococci. A study of the former compounds is being carried out by Morgan in Britain (Morgan, 1944).[a]

[a] [*BMB* 422 & 555]

One of the factors that has held up the progress of biochemical genetics has been that only reactions involving relatively-simple compounds have been susceptible of analysis. Advances in our chemical knowledge of proteins, nucleic acids and polysaccharides cannot fail to provide chemical genetics with new methods and new sources of information.

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were surprised to find that the filtrate still produced symptoms of disease. Although well aware of the high dilution at which foot-and-mouth lymph is infective, they argued that the effect could not be due to a toxin because the lymph from animals that had been inoculated with a filtrate produced symptoms. As an alternative they suggested that the agent, although small enough to pass through the pores of the filter, multiplied in the affected animal. They also suggested that a group of other diseases might have a similar cause. In the same year, the significance of passage through a porcelain filter was also fully appreciated by Beijerinck (1898). He filtered tobacco-mosaic virus and also demonstrated the diffusion of the infective agent through agar gels. These experiments led him to suggest that the agent was not " corpuscular " but was what he called *contagium vivum fluidum.*

1. Size as a Criterion

It is not easy, at the present time, to understand what precise distinction, other than the purely quantitative one of particle-size, Beijerinck was making. Atomic theories were already 2,400 years old, and the atomic and molecular conception of matter had achieved general acceptance during the 19th century. The reality of atoms was, it is true, still doubted by Ostwald and other members of the " Energetics " school, but more perhaps as a logical exercise than as a matter of practice. Clerk Maxwell spoke confidently, in an article in the Encyclopaedia Britannica (1875), of their reality, and even made some estimates of the number of molecules in the smallest organisms and emphasized the bearing of this subject on current theories of heredity. However, as late as 1909, Perrin entitled his masterly survey of the various independent methods by which Avogadro's number could be determined " Mouvement brownien et réalité moleculaire ". When Beijerinck wrote, the nature of matter was in doubt, and even those who believed in molecules were uncertain of their size. Biologists at that date may therefore be forgiven for imagining that a fundamental qualitative difference existed between the corpuscular or particulate and the soluble or fluid states of matter; there is less excuse for the traces of the same belief that still linger in the writings of some pathologists.

Filtration through a candle was established as a practically-useful, but arbitrary, upper size-limit to the group of viruses. This was at first expressed in the phrases " filtrable microbe " or " filtrable virus ", but usage and the fact that diseases resembling the virus-diseases in other ways are sometimes not transmissible by filtrates, has led to the adoption of the simple word virus to cover this ill-defined group. There is no rigid boundary between the large viruses and the small bacteria, and a discussion on the correct category for an agent like that of pleuropneumonia might have value in law but has none in science. The lower limit of size is equally uncertain. The factors causing capsule-formation in rough strains of pneumococci are generally looked on as " substances " rather than viruses, but this distinction is not logical. Transformation is associated with the production of more of the factor, so that one has the phenomenon of multiplication of the factor in susceptible organisms. Avery, MacLeod & McCarty (1944) have evidence that transformation is due to a polymerized nucleic acid. The possibility of virus-like action with simpler substances remains open. Plant-galls can be produced by treatment with auxins; if the gall were itself rich in auxin, the state of affairs would be formally indistinguishable from an infection. An extract of the anomalous tissue would produce more of the characteristic anomaly when put on to healthy susceptible tissue. No example of this phenomenon is yet known, but it may be confidently predicted that examples will be found and that the effective auxins will be synthesizable. There will then be a smooth gradation, without any qualitative break, from synthesizable molecules at one end to microscopically-visible organisms at the other.

2. The Physico-chemical Approach

In the first quarter of this century the problem had been defined, certain infective states were classified as virus-diseases, and limits could be put to the size of the effective agents. It was not immediately obvious that the nature of a virus was a suitable theme for biochemical investigation, because our knowledge of the sizes of other biologically-important colloids was still meagre. It is unlikely that anyone giving serious thought to the matter doubted that viruses contained protein, because the unique role of proteins in biological phenomena had long been accepted; but protein-sizes had not been measured. Some tentative figures were derived from the elementary composition of proteins, especially from the iron content of haemoglobin, but it was not until the decade 1920–30 that osmotic pressure and ultracentrifugal measurements gave figures of generally-accepted validity.

The narrowing of the gap between the larger proteins and the smaller viruses stimulated many workers to investigate viruses from a chemical or physico-chemical standpoint. Two early purifications, that of vaccinia virus by Craigie (1932) and of a *Bact. coli* virus by Schlesinger (1933, 1936), were outstandingly successful. These viruses lack the geometrical or electrical simplicity that is a prerequisite for crystallization or the exhibiting of other striking physical properties, but it is probable that the preparations made in 1932 contained as high a proportion of active virus in the original state as most virus-preparations that have been described since. They were certainly more fully entitled to the designation " pure virus " than any plant-virus preparation made before 1940. Several attempts to purify tobacco-mosaic virus were made. Barton-Wright & McBain (1933) tentatively identified it with a protein-free crystalline material that they made from infective plant-sap. This suggestion was received sceptically by biochemists. A more confident identification by Stanley (1935) was at first similarly received. This scepticism was fully justified, for all the novel properties ascribed by Stanley to his crystalline globulin have proved not to be properties associated with the virus. The properties that are now accepted as those of tobacco-mosaic virus in its aggregated state were set out by Bawden, Pirie, Bernal & Fankuchen (1936) and were more fully defined by Bawden & Pirie (1937a) and by Bernal & Fankuchen (1941). Stanley has, from time to time, incorporated these properties in his description of the virus. This promotes unanimity but leads to the impression that his early description was confirmed rather than contradicted. Some parts of the description, e.g., the formation of tactoids in strong neutral solution, and fibres or " para-

crystals" rather than true crystals on precipitation with acid or on salting out, were accepted by Stanley almost immediately. Other parts were accepted more slowly, e.g. the invariable presence of nucleic acid in active preparations (Loring & Stanley, 1937; Stanley & Loring, 1938), and then only after argument (Bawden & Pirie, 1937b). The properties found with these early preparations are those of aggregates (Bawden & Pirie, 1937a; 1938c; 1946); this very important point has not yet been accepted by Stanley. It will be referred to more fully later. The sap of plants infected with various other viruses has yielded characteristic nucleoproteins which are either the viruses or are related to them. Some of these resemble tobacco-mosaic virus in forming liquid crystals, e.g. potato X (Bawden & Pirie, 1938a) and potato Y (Bawden & Pirie, 1939); others form true three-dimensional crystals, e.g. bushy stunt (Bawden & Pirie, 1938b), tobacco necrosis (Pirie, Smith, Spooner & McClement, 1938; Bawden & Pirie, 1942) and turnip yellow mosaic (Markham & Smith, 1946).

3. Microbes or Molecules?

The preparation of so many plant-viruses in forms with characteristic chemical and physical properties has fostered two unfortunate illusions: that there is a qualitative distinction between plant- and animal-viruses and that plant-viruses have been shown to be substances or molecules rather than organisms. More than 200 plant-viruses or virus-strains are known, and only about 20 have been subjected to serious chemical or physical study. These have been selected for detailed study largely because they give a highly infective sap, which retains its infectivity in spite of the various changes that go on in ageing leaf-extracts. These are more or less chemical criteria, and any uniformity which appears to run through the group of plant-viruses is at least as likely to be due to this initial selection as it is to be due to a genuine uniformity in the viruses. Animal-viruses have, from a chemical point of view, been chosen at random; that is to say they have been chosen for their social or economic importance. Those so far investigated, notably by Beard and his associates, have tended to be larger and more complex chemically than the plant-viruses, but it would be premature to make any generalizations until many more have been investigated.

The distinction between molecules and organisms, in any region where this distinction could be uncertain, is purely verbal. In so far as it can be defined, it is between materials that are handled by the methods characteristic of a biochemical laboratory and materials handled by methods characteristic of a biological laboratory. But many well-known materials are habitually handled in both ways. We all agree that *Bact. coli* is an organism, but when it is being disintegrated to make an enzyme-preparation or hydrolyzed as a prelude to amino-acid analysis, it is being treated as a substance and, but for the preliminary agreement, might be looked on as a molecule. The position with viruses is similar. No one has demonstrated that some of them are substances or macromolecules. Indeed, such a thing is not susceptible of demonstration; it is not a statement about the viruses but about the mental approach and technique of the research-worker. It has, however, been amply demonstrated that, as Beijerinck suspected, valuable information about their properties can be won by the methods of biochemistry.

Valuable as the contributions of biochemistry to the study of viruses have been, they are not without danger. The application of some chemical methods to the study of a group of substances does not guarantee the amenability of these substances to all other chemical criteria. Uniformity is the most important of these. In the study of the simpler molecules, on which the main structure of chemistry rests, any difference in composition between two molecules is quantitatively significant because the weight of an atom is an appreciable fraction of that of the molecule. Even the smaller proteins are so large that this is no longer true, and the replacement of one amino-acid residue by a different but similar one would not be detected by any of the elementary analyses or physical measurements so far made. *A fortiori* such a replacement would not be detectable in a virus. In the absence of any possibility of demonstrating that all the particles in a virus-preparation are identical, there seems to be little point in asserting that they are molecules. The only effect of this assertion is to rob a useful word of the meaning that it has in the more rigid discipline of chemistry. As soon as a particle has become so big that the introduction of, for example, a $-CH_2-$ group has no longer an observable effect on the particle-size or analytical composition, the word molecule has become misleading (cf. Pirie, 1940; 1946). Clerk Maxwell (1875) distinguished clearly the use of the word by chemists, to mean identical primary particles of a substance, from the use by physicists, to mean a particle in a fluid that did not break up during the observation. This distinction is in danger of being disregarded, and the demonstration of physical molecularity is loosely taken to imply chemical molecularity as well.

The argument in the preceding paragraph is designed to show that, even if successive preparations of the same virus from different sources cannot be shown either to differ from one another or to be inhomogeneous, there is still no basis for the claim that all the particles are identical in the sense that those of, for example, sucrose are. Such an argument is not, strictly speaking, necessary, for even those viruses for which the molecular claim has been made most persistently are demonstrably variable and inhomogeneous. The particle-weight and analytical composition attributed by Stanley and his colleagues to tobacco mosaic have ranged over a wide field. Even in the same paper different values may be given; thus Gaw & Stanley (1947) quote phosphorus-values, one of which is 25% higher than the other, as evidence that a strain of tobacco-mosaic virus is the same when grown on tobacco as when grown on phlox. It is unlikely that such evidence would be acceptable in other fields of chemical research.

It is clear, both from first principles and from a consideration of the type of evidence that is actually published, that the idea of viruses as molecules in the strict chemical sense is misleading. Beard (1945; Hook *et al.* 1946) has ably presented the case against regarding some of the animal and bacterial viruses as molecules. He tends to contrast them, because of their variability in composition and particle-size, with the plant-viruses and other materials often classified as macromolecular. An experience of a fairly wide range of these substances, including plant-viruses, proteins, bacterial antigens, agar and hyaluronic acid, suggests that this distinction is unreal. The variability of these substances may not be so great as that of the

viruses which Beard has studied, but the difference is quantitative only.

4. Nature of the Fundamental Virus-Particles

Variation between individual virus-particles or between successive preparations of the same virus can arise in many ways. There is no *a priori* reason why the property of being virus, that is to say of transmitting a certain set of symptoms or behaving in some other defined way, should be associated with a unique chemical structure. The virus-building mechanism may make a range of products, all active and similar, but not identical. It is equally probable that initially-identical particles should become non-uniform through association, dissociation, or the adsorbtion of components from the environment. Bawden & Pirie (1945) have some evidence that the last two processes operate to control the properties of tobacco-mosaic virus. In their view, the free virus aggregates in solution, but this aggregation can be prevented by other adsorbed materials. They suggest tentatively (1937a, 1945) that the primary particle is more or less spherical and smaller than the rods which are the predominant constituent of old or roughly-handled virus-preparations. Stanley stoutly defends the position that the rods, which Bawden and Pirie had described, are the fundamental particles, and that all others are derived from them. He has (Oster & Stanley, 1946; Sigurgeirsson & Stanley, 1947) published electron-micrograms purporting to show the original state of the virus in the cell. His technique, however, involves exposing the virus to that unphysiological fluid "leaf sap" which, as Bawden & Pirie (1945) have demonstrated, is a powerful aggregating agent. Furthermore, there are serious limitations to the use of electron-micrograms in getting evidence of this type (cf. Pirie, 1945; Crook & Sheffield, 1946). Stanley's position has the obvious merit of simplicity, but this simplicity can be achieved only by disregarding much of the available evidence.

5. Combination of Virus with Tissue-Constituents

The presence of material, attached to the particles in a virus-preparation but not essential for the activity of the preparation, has been recognized with many other viruses. Curnen & Horsfall (1947, and earlier papers) have studied the complex that the pneumonia virus of mice makes with a constituent of lung and other tissues. Free virus can be made, and this will then combine with the tissue-constituent in vitro. It therefore seems probable that the complex is an artefact made during the extraction of lung by the original methods as a result of bringing together components not normally in contact in the tissue. Influenza-virus preparations contain material reacting with antisera against chick-embryo or mouse, depending on which host has been used for cultivating the virus (Knight, 1946). Virus free from these components has not yet been made, and it is therefore not possible to say whether, here also, the complex is an artefact, or whether some components of the host are essential for the stability of the virus-particle. Cohen (1946) has described a phenomenon in the T2 virus of *Bact. coli* which may have a similar origin. When grown on a synthetic medium, the virus is associated with extra desoxyribose nucleic acid and this can be removed from it, without loss of virus-activity, by digestion with desoxyribonuclease. Here, therefore, an apparently homogeneous virus-preparation contains material inessential for virus-activity. There is no evidence showing whether it has any relationship with normal host-cell components or not. The tumour-viruses give many examples of similar phenomena. Carr, for example, has good evidence (1944) that the antibodies, built up in an animal carrying a Rous No. 1 sarcoma, progressively reduce the filterability of the tumour-virus, presumably by precipitating it in the interstices of the tissue. The only apparent difference between this and the other examples of complex-formation quoted is that the complex never appears in suspension. There is no evidence for anything analogous to antibody-formation in plants; it is therefore unlikely that precipitation of this type explains Bawden & Pirie's (1946) observation that the greater part of the virus in plants with tobacco-mosaic is not in solution but firmly attached to the structure of the leaf. If this phenomenon is at all general, it greatly widens the field of complex-formation.

6. Conclusions

In recapitulation it may be said that our ideas about the nature of viruses are now based on much information, but that this has increased rather than diminished the complexity of the subject. It is a matter of observation that there is no clear demarcation between viruses and bacteria, and there is probably no demarcation between viruses and physiologically-active but synthesizable molecules. All the viruses purified so far have contained nucleoprotein, but this generalization may lack significance because the viruses that have been studied are a group selected to some extent on a chemical basis. Furthermore, the purified virus is the minimum unit capable of starting the infective process in a susceptible cell. It may well be that an essential preliminary to the process of multiplication is the accretion to the virus of various other cell-constituents. This view has for long seemed probable *a priori* (cf. Dale, 1935); the frequency with which viruses, if isolated by gentle procedures, are associated with host-cell constituents is confirmatory evidence for it. It becomes a matter of arbitrary definition at what point, in stripping away host-components from a virus, one is purifying it, and at what point one is modifying it. These considerations need emphasis because of the frequency with which the supposed facts of virus-research are used in discussions on other branches of biology. There are clearly resemblances between viruses and genes (Muller, 1922) or other tissue-components (Claude, 1941) but caution is necessary in arguing from these resemblances. In commenting on the position it would be difficult to improve on Beard's (1945) felicitous phrase: "Viruses are said to be living molecules and autocatalytic enzymes and are likened to genes and mitochondria—in short, a fabric of concepts has been woven of a plethora of woof with a paucity of warp."

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CONTRIBUTIONS OF CHEMISTRY TO THE PROBLEMS OF IMMUNOLOGY

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1 Mechanisms of immunity
2 Antigens and their immunological specificity
3 Chemically-altered and conjugated protein-antigens
4 Bacterial and other cell-antigens
5 Blood-group substances
6 Antibodies and the antigen-antibody reaction
7 Inhibition tests (competitive inhibition)
8 Hypersensitivity or allergy to simple chemical compounds
9 Complement
10 Miscellaneous
11 Possible future developments
References

This is a not inopportune time for a review of the present position of immunochemistry and of the contributions that chemistry has made to this branch of science. The phenomena of immunity are essentially chemical, and we might reasonably expect that some of its problems will soon be solved if a more sustained chemical and biochemical attack is made on them.

Ehrlich can be credited with some of the earliest efforts to apply the principles of chemistry to immunity. He believed that the combination of toxins with animal cells on the one hand, and with antitoxins on the other, were processes which obey the ordinary laws of chemistry and physics. His "side-chain" theory, with its toxophore, haptophore and other receptor groupings, certainly became very complicated in the various modified forms which were developed to meet objections to his theory, but at least it gave stimulus to an immense amount of discussion and scientific investigation; above all, it gave a pictorial conception of the interaction of antigen and antibody by chemical reactions. These views were, however, strongly opposed by Bordet, who maintained that immune reactions take place as a result of physical or colloidal processes, with emphasis on adsorption. The comforting terminology of the early colloidal chemistry satisfied most immunologists for a long time, and, as Heidelberger (1946) aptly remarked, "many of those who once found it useful and comfortable still think of it with nostalgia". Evidence of this can readily be obtained from many textbooks of pathology and bacteriology, but it must be recorded with regret that in 1927 a well-known biochemist, surely in a moment of mental aberration, subscribed to the view that complement may merely be a name for a physical state of the serum.

During the past two or three decades the position has shown material improvement, in the eyes of the chemist, thanks to the efforts of such men as Arrhenius, Wells, Landsteiner, Zinsser, Heidelberger, Avery, Marrack and a host of others, who have tried to think of immunology in terms of chemistry. Above all, Landsteiner might perhaps be regarded as the father of modern immunochemistry. Wells' *Chemical aspects of immunity* (first published in 1924 and revised in 1929) was certainly a milestone recording progress in the development of this subject, and giving encouragement to those who had just joined the pilgrimage, but it was largely the laboratory investigations of Landsteiner over the period 1906-43 which formed the basis of our knowledge of immunological specificity. As befitting one who had served an apprenticeship in Emil Fischer's laboratory, Landsteiner was able to think of antibody formation and the reactions between antigen and antibody in terms of organic

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chemistry; and the modern concept of the chemistry of serological specificity rests largely on his work and the work of those who followed his example. Avery and Heidelberger, with their isolation of the specific polysaccharides of the pneumococcus, and Heidelberger and his colleagues, with their use of analytical chemical methods for the study of antigen-antibody reactions, have done much to provide rational explanations for many immunological phenomena.

1. Mechanisms of Immunity

The chemist is particularly interested in the structure and composition of antigens and antibodies. A "true" or full antigen is a compound which on injection into an animal produces antibodies capable of reacting specifically with the antigen, e.g., by precipitating or agglutinating it. Certain polysaccharides and some other non-protein compounds, which, although incapable of inducing any marked antibody-formation when injected, can react in vitro with specific antibodies, are termed haptens (Landsteiner), and much information about the chemistry of immunity has come from the study of these compounds.

The view is widely held that antibodies may be the real key to immunity, but it also seems probable that some or all of them may act in collaboration with the phagocytes. Precipitation or agglutination of the bacteria or foreign substance may not actually occur in vivo, but there appears to be no doubt that chemical combination of antigen and antibody does take place in the animal body; the elimination of the precipitated or "neutralized" material requires the help of phagocytic cells, complement, and possibly other non-specific defence-agents of the body.

The study of phagocytosis has not been neglected by chemists (cf. review by Mudd, McCutcheon & Lucké, 1934), and the opsonins which facilitate and promote phagocytosis have also been investigated. There is, however, the need for a renewed attack on phagocytosis and opsonic action with the more modern weapons of chemistry.

In recent years, much interest has been shown in other non-specific resistance-factors of the tissues, such as leucotaxine (causing leucocyte emigration to the infected area), hyaluronic acid, hyaluronidases ("spreading" or "diffusing" factors), and lysozyme. Leucotaxine, described by Menkin (for the literature, see Hadfield & Garrod, 1942, and Boyd & Malkiel, 1947) has been isolated as a crystalline and extremely potent product having the properties of a polypeptide. Hyaluronic acid, present in certain bacterial capsules, is a polymer of acetyl-glucosamine and glucuronic acid, and the enzyme hyaluronidase has been obtained in a highly purified form and its polysaccharide-splitting activity fully studied. Lysozyme, which is widely distributed in nasal secretion, saliva, tears, leucocytes, and egg-white (Fleming, 1922) has been isolated as a crystalline protein (Abraham & Robinson, 1937; Alderton, Ward & Fevold, 1945); it has a molecular weight of about 17,000, and an iso-electric point between pH 10.5 and 11.

The immunological role of hyaluronic acid and hyaluronidases, and the significance of the production of hyaluronic acid by some bacteria, and of hyaluronidase by others, have yet to be elucidated. The functions of lysozyme are also not yet established, for most pathogenic organisms show little if any susceptibility to its action. The chemist has, however, paved the way to a full-scale attack by exposing some of the mysteries of these tissue- and cell-defences; now that many of these resistance-factors are becoming available in a chemically pure state, there is a much greater hope for success in the study of these problems.

2. Antigens and their Immunological Specificity

Since most full antigens are proteins or protein-containing complexes, it is not surprising that the serological specificity of proteins has been extensively studied. As a result of this work (cf. reviews by Landsteiner, 1945; Boyd, 1943), we know that this specificity depends on the chemical structure of the antigens. It is not always possible by laboratory methods to detect chemical differences between two closely-related natural proteins which the rabbit can readily distinguish by producing antibodies which react with one protein and not with the other; but more refined chemical technique will almost certainly render this possible. Chemistry has undoubtedly made valuable contributions to our knowledge of antigen and antibody specificity, and much greater progress should be made in the future by closer collaboration between biochemists and immunologists.

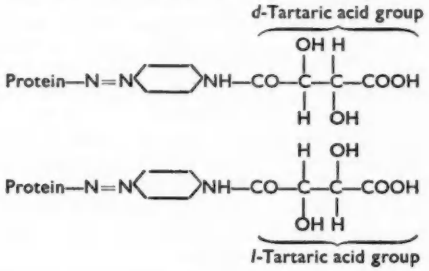
Immunological activity is, of course, not confined to the proteins, for the specificity of certain bacterial and other cells is largely due to carbohydrates and carbohydrate-lipid complexes. Some purified lipids can also act as specific antigens. In all these cases a chemical attack has been made, and much useful information has been obtained about the chemical groups responsible for the serological specificity of these antigens.

3. Chemically-altered and Conjugated Protein-Antigens

An extensive study has been made of the specificity of protein-antigens by the attachment of various well-defined groups to proteins to produce complexes having serological properties different from those of the original protein. The most successful method, and one which has been used by numerous workers, is that introduced by Landsteiner & Lampl (1917); it involves the use of a compound containing a diazotizable amino-group and the coupling of the diazotized compound with a protein to form an azoprotein complex. Studies on a wide variety of azoproteins have shown that this conjugation gives the protein a new specificity dependent on the "determinant" group introduced, and on the spatial configuration in that group. A full account of these investigations is given by Boyd (1943), Marrack (1938) and Landsteiner (1945), and all that is possible here is a brief reference to a few fundamental discoveries. Landsteiner & van der Scheer (1932, 1934, 1939) attached peptides containing 2 to 5 amino-acid molecules to proteins, and found that although the specificity of these conjugated proteins was partly due to the nature, order, and the number of the amino-acid molecules attached, the predominant influence was exerted by the amino-acid at the free end of the peptide chain. Shortly before this, the same authors (1928) found that serological tests could readily differentiate between the *d* and *l* isomers of phenyl-(*p*-aminobenzoylamino) acetic acid and in a more striking way the isomers of tartaric acid (1929). In the latter case, the immunized rabbit differentiated sharply between azoproteins which differed only in the arrangement of the H and OH groups in the tartaric acid portion of the tartranilic acid linked to the protein. Fig. 1

indicates diagrammatically the delicacy of this serological differentiation.

FIG. 1. TARTARIC ACID AZOPROTEINS



Steric isomers of this type were also studied by Avery & Goebel (1929), who obtained serological differentiation between azoproteins containing glucose and those containing galactose. In further investigations on these carbohydrate-azoproteins, Goebel (1940) succeeded in immunizing mice against pneumococci of Types II, III and VIII by injecting into them antisera towards azoproteins containing cellobiuronic acid (a disaccharide containing one molecule of glucose and one of glucuronic acid). This production of an effective immunity towards an actual disease by the use of an artificial antigen containing a synthetic hapten marked a distinct advance in immunochemistry.

In more recent years Harington has introduced the use of the reaction between azides and the free amino-groups of proteins to produce conjugated proteins in which the haptenic group is linked to the protein by a peptide linkage. This elegant method (Clutton, Harington & Mead, 1937 ; Clutton, Harington & Yuill, 1938) has been successfully used for the production of antisera against thyroxine (for the references cf. Harington, 1944a) and aspirin (Butler, Harington & Yuill, 1940).

Protein specificity has also been studied by the direct introduction of atoms or small groups into the protein molecule, this process usually inducing in the protein a new specificity characteristic for the grouping introduced (cf. reviews by Landsteiner, 1945 ; Wells, 1929 ; Wormall, 1937). In this way, useful information has been obtained about immunological specificity, and indirectly about the structure of proteins. The actual determinant groupings in natural protein-antigens is not yet known, but the nature and order of the amino-acids in the polypeptide chains undoubtedly has a decided influence. The carbohydrates naturally linked to egg-white proteins do not appear to play any part in determining the serological specificity of these glycoproteins (Neuberger & Yuill, 1940).

4. Bacterial and other Cell-Antigens

Important progress has been made in the investigation of the chemistry of the antigenic mosaic of the bacterial cell. In many instances the components of these antigenic complexes have been separated and identified, and their biological action investigated, and this field of immunological research has been " one of the most fruitful in discoveries of both theoretical and practical importance " (Dubos, 1945, p. 234).

The chemical nature of bacterial antigens has been well reviewed in this journal by Morgan[1] (1944a), with an account of typical haptens and antigens from some gram-positive and gram-negative organisms. Considerable progress followed the separation by Boivin and his colleagues in 1933 (for the literature, cf. Morgan, 1944a ; Landsteiner, 1945), and by Raistrick & Topley (1934), of highly antigenic complexes containing specific polysaccharides and lipids.

The more-recent use of special reagents for the separation and partial degradation of the complexes has yielded non-antigenic undegraded specific polysaccharides and non-antigenic phospholipin - polysaccharide complexes. For example, Morgan & Partridge (1941, 1942 ; cf. also Morgan, 1943) have obtained evidence that the protein component of the phospholipin-polysaccharide-protein antigen isolated from *Bact. dysenteriae* (Shiga) and *Bact. typhosum* is a conjugated protein, and Freeman (1943) has obtained an antigenic complex from *S. typhimurium* which is believed to be a chemical entity ; this complex contains specific polysaccharide (69 %), a conjugated protein (16 %), mixed lipids (3-4 %), and an alcohol-soluble acetylated polysaccharide (about 8 %).

To establish the exact constitution of an organic compound the chemist first analyzes it, and then splits it into its component pieces. A provisional formula might then be given to the compound, but final proof of this formula usually awaits synthesis of the compound from simpler substances of known constitution. As a natural corollary to the analysis of bacterial antigens, attempts have therefore been made, with considerable success, to re-combine the isolated polysaccharide and the conjugated protein, and thus to form complexes which are antigenic and which produce antibodies specific for the polysaccharide component. In a similar way, other non-antigenic polysaccharides, and the haptenic specific blood-group agglutinogens A and B, have been converted into full antigens by combination with a bacterial somatic conjugated protein (cf. Morgan 1943, 1944a).

Amongst other observations of special interest to chemists is that of Avery, MacLeod & McCarty (1944). These authors isolated from Type III pneumococcus a polymerized desoxyribonucleic acid which, when added to a medium in amounts as low as 1 part in 6×10^8, can effect the transformation of Type II pneumococcus into Type III, a change of specificity which is permanently retained by the organism.

5. Blood-Group Substances

Much information has been obtained (cf. Morgan, 1944b[2], 1947 ; Witebsky, 1946) about the chemical nature of the blood-group substances A, B and O, particularly the A substance, since it can readily be prepared on a large scale from hog gastric mucosa. The highly potent purified A substance contains 5.7—6.4 % N, 9.2—11.5 % acetyl and 27 % hexosamine (Morgan & King, 1943). Purified preparations of these group-specific substances have been used to reduce the anti-A (or anti-B) titre of group O blood to be used for transfusion (Witebsky, Klendshoj & Swanson, 1941), and also for injection into man to produce strong grouping-serum (Witebsky, Klendshoj & McNeil, 1944).

[1] [*BMB* 555]
[2] [*BMB* 422]

6. Antibodies and the Antigen-Antibody Reaction

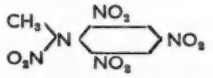
Antibodies have been shown to be adapted or slightly modified serum-globulins, and their combination with various antigens in the precipitin reaction has been studied quantitatively by many workers, notably by Heidelberger and his colleagues. From chemical analyses of antigen-antibody precipitates a quantitative theory of the precipitin reaction was developed (Heidelberger & Kendall, 1935, and later papers; cf. reviews by Heidelberger, 1939, 1946; Kendall, 1942). The data obtained support the view that both antigen and antibody are multivalent, thus giving strong quantitative support for the "lattice" or "framework" theory of Marrack. Space does not permit further discussion of these fundamental analytical investigations, and of the equations and formulae developed to give a quantitative expression to the precipitin- and other immune reactions, but the reader is referred to the stimulating and provocative reviews by Boyd (1943), Pauling (1940) and Pauling, Campbell & Pressman (1943). Useful accounts of the applicability of quantitative methods in immunochemistry are given by Kabat (1943) and Treffers (1944), and the nature, properties and formation of antibodies have been reviewed by Marrack (1942) and Haurowitz (1947). Methods for the quantitative determination of antibodies are now fully established (cf. Heidelberger, 1946), and according to Dubos (1945, p. 272) this ranks as "one of the great achievements of immunochemistry".

7. Inhibition Tests (Competitive Inhibition)

Modern investigations in chemotherapy have been largely re-orientated since the recognition that many bactericidal compounds, narcotics, and other drugs act by competition. It is often overlooked, however, that competitive inhibition in enzyme systems had been studied at an earlier date, and that the specific inhibition of serological reactions had also been described. Landsteiner (1920) showed that simple substances having structures identical with, or similar to, the hapten group of azoproteins could specifically inhibit the reaction between the azoprotein and its antiserum. Since that date, serological inhibition-tests have been used very extensively (cf. reviews by Marrack, 1938; Boyd, 1943; Landsteiner, 1945) and valuable information has thereby been obtained about the "determinant" or serologically-dominant groups in many antigenic complexes and chemically-altered proteins, and about serological specificity in general. This inhibition-test technique greatly simplified many immunochemical studies and greatly widened the field of investigation. Work carried out in Landsteiner's laboratory showed, for example, that the specificity of iodinated-protein antigens is due to the 3 : 5-diiodotyrosine groupings (Wormall, 1930). Proof that the inhibiting compounds actually combine with the antibodies was obtained by Marrack & Smith (1932), and later by Haurowitz & Breinl (1933).

8. Hypersensitivity or Allergy to Simple Chemical Compounds

The acquired hypersensitivity of an individual to a protein or a protein-containing complex might be explained by assuming that previous exposure to the material had produced antibodies which rendered the subject specifically allergic or hypersensitive to the "allergen". Hypersensitivity to simple compounds ("drug allergy") could not be so readily explained, until it was gradually realized that the exciting agents might have been rendered fully antigenic by combination with the body-proteins to produce new protein-complexes which were "foreign" and therefore antigenic to the body. Full confirmation of this view has been obtained by various workers, and Landsteiner & Jacobs (1935) were able to sensitize guinea-pigs with dinitrochlorobenzene, picryl chloride, and many other comparatively simple aromatic compounds, several of which are known to produce hypersensitivity in man. Various workers have obtained further evidence of this formation of antigenic conjugates (cf. Landsteiner & Chase, 1937a, 1937b, and the review by Landsteiner, 1945); and Harington (1944b) and his colleagues have succeeded in sensitizing guinea-pigs to tetryl, and have obtained evidence that the sensitization is due to the action of the tetryl on the skin-proteins.



Tetryl

All types of drug allergy cannot, of course, be accounted for on the basis of combination of the drug with body-proteins to form a "foreign" protein. There is, however, an increasing amount of evidence that the ordinary protein molecule contains a variety of very reactive groupings, and that it can combine with many compounds which chemically are regarded as very inert; the trypanocidal drug suramin (Bayer 205), for example, firmly combines with serum- and other proteins (Dewey & Wormall, 1946). Thus it seems possible that immunochemical studies, and others concerned with the interaction of drugs and proteins, may help to throw some light on drug allergy.

9. Complement

Not many years ago complement was regarded as one of the insoluble mysteries of immunity, and the specific lytic action of this reagent or system was often referred to as a special physical property of the serum (for the early literature see Osborn, 1937). At last the faith of many chemists is gradually being justified, for three of the four known components of complement have now been isolated in a highly purified form. Many authorities regard complement as a keystone in the immunity defence-systems of the body, and a clearer knowledge of this agent should undoubtedly greatly improve our chemical knowledge of immunology. Work in this field has been greatly stimulated by the use of the more-refined methods of physical chemistry by, amongst others, Ecker and Pillemer (cf. Ecker & Pillemer, 1942; Pillemer, 1943) and Heidelberger. Exact details have been given (Bier, Leyton, Mayer & Heidelberger, 1945) for the titration of the four individual components of complement, and from many laboratories useful information is forthcoming about the chemical properties of these components and their role in serological tests (cf. reviews by Marrack, 1942; Kabat, 1946). Perhaps we shall not have to wait long now before we learn the chemical mechanism underlying the specific destruction of the fourth component of complement by ammonia and ammonium salts, and the specific adsorption or inactivation of the third component by an insoluble yeast-carbohydrate. We might also find the answer to the question as to whether one of the components is an enzyme and another a lipid.

10. Miscellaneous

There are many other branches of immunochemistry where vigorous chemical attack has been, and is being made, with considerable success. It will merely be possible here to mention a few reviews and other publications, and perhaps the reviewer will be forgiven if this selection is considered rather arbitrary and haphazard. Reviews and discussions on anti-hormones (Thompson, 1941), anti-enzymes (Sevag, 1945), the production of antisera against thyroxine (Harington, 1944a), the chemistry of viruses (Andrewes[3], 1944; Pirie[4], 1946), nutrition and resistance to infection (Schneider, 1946) and several papers on the production of antisera against the "sulpha" drugs, various antibiotics and carcinogenic compounds, indicate some of the problems which have interested immunochemists. Isotopic tracers are also being used to study immunity (Schoenheimer, Ratner, Rittenberg & Heidelberger, 1942; Heidelberger, Treffers, Schoenheimer, Ratner & Rittenberg, 1942; Boursnell, Dewey, Francis & Wormall, 1947), and immunochemical methods have been used to study the action of mustard gas on proteins (Berenblum & Wormall, 1939; Boursnell, Francis & Wormall, 1946). Pauling (1945) has given an excellent account of molecular structure and intermolecular forces in relation to immunity, and a modern claim has been made (Pauling & Campbell, 1942a, 1942b) that antibodies can be made artificially in the test-tube. Northrop (1942) has isolated a crystalline diphtheria-antitoxin.

11. Possible Future Developments

The reactions of an immunochemist who might happen by chance to glance at this review 30 or 50 years hence are difficult to anticipate. They are fairly certain to be somewhat critical, but nevertheless the temptation to speculate on possible future developments in immunochemistry is too great to be resisted by the present reviewer. It seems probable that more of the "heavy guns" of chemistry and physics will be brought into action, and that more of the modern weapons, including radioactive and stable isotopes, will be brought into play. The USA, by virtue of its good fortune in having large supplies of these special isotopes available for tracer work, will almost certainly take a leading part in these investigations. Just as the isotopic-tracer method has solved some of the most complex problems of biochemistry, so it should help to explain some of the mysteries of immunity.

Further advances might also be expected by the use of antibodies against vitamins, enzymes, hormones, and drugs of special chemotherapeutic interest. Immunochemical methods might, for example, throw some light on the production of drug-resistant strains of micro-organisms, and if there is an undue development in nature of these drug-resistant strains, more reliance might have to be placed on immunological methods of treatment. Another possible development is the extended use (perhaps therapeutic) of nucleic-acid derivatives, similar to that isolated by Avery and his colleagues, for the transformation of organisms into less-virulent strains, and for producing mutations of micro-organisms for biological investigation.

More chemical information about the blood-group factors, including the Rh factors, should almost certainly be obtained before very long, and this might help considerably towards solving some of the remaining problems of haemagglutination in blood-transfusion and pregnancy.

There are many other avenues which are fairly certain to be explored, but sufficient has been said here to indicate a few of the contributions which chemistry has made, and will make, in the study of immunology. It might also be claimed that immunochemistry has a double role, for even as the chemist can assist in revealing some of the mysteries of immunology, so can immunological methods be profitably used to study some of the general problems of biochemistry.

[3] [*BMB* 551]
[4] [See also *BMB* 1201 in this number.—ED.]

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In a short review of this type it is impossible to quote more than a small fraction of the literature. For more-comprehensive surveys, the reader is referred to the reviews of Boyd (1943), Hartley (1931), Heidelberger (1938), Landsteiner (1945), Marrack (1938), Sevag (1945), Topley & Wilson (1946), and Wells (1929). Valuable up-to-date articles are given in the *Ann. Rev. Biochem.*, some of these being mentioned below; others are by Chase, M.W. & Landsteiner, K. (1939, **8**, 579) and Heidelberger (1932, **1**, 655; 1933, **2**, 503; 1935, **4**, 569).

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FIBROUS PROTEINS AS COMPONENTS OF BIOLOGICAL SYSTEMS

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1 Types of fibrous protein
2 Soluble fibrous proteins
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The manifestations of life arise from a multitude of chemical reactions which are accelerated by a corresponding variety of protein molecules, the biological catalysts which we call enzymes. In this respect, life and catalysis are synonymous terms. For most people, the great ingenuity of these reactions, and their importance in metabolic processes, excite much more interest than the nature of the molecules which catalyze them. This is not at all surprising, since the nature of an enzyme is wrapped in the greatest problem which confronts mankind—the elucidation of protein structure.

As far as we know, most enzymes, and therefore most proteins, are corpuscular, and an exact formulation of their structure demands a knowledge of the number of separate peptide chains in the molecule, the sequence of amino-acids along the chains (which are not themselves necessarily identical), the way the chains are folded, and the manner in which the folded individual chains are brought together to form the native protein molecule. It is recognized that certain patches on the molecule, consisting of a precise arrangement of chemical groups, are responsible for enzyme activity and for the specificity of the catalyzed reaction. In many enzymes, sulphydryl groups participate in this spatial array of groups, but others are also involved. The existence of such groupings raises another fundamental problem of the structure of proteins: whether they arise by the manner of folding of the peptide chain, or from a formalized fold by the sequence of amino-acids along it. Such questions have a teleological flavour until the mechanism of protein synthesis is elucidated.

1. Types of Fibrous Protein

In the light of these immense problems, it has seemed more profitable to investigate those types of proteins which, superficially at least, are not quite so complex. These are

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the fibrous proteins, in which the polypeptide chains are fully, or almost fully, extended, as in collagen (Astbury, 1940), silk, feather keratin (see Astbury & Bell, 1939); or show a regular and probably simple type of fold as in epidermal appendages (hair, horn), the epidermis itself (Rudall, 1946), fibrinogen (Bailey, Astbury & Rudall, 1943), myosin (Astbury & Dickinson, 1940) and tropomyosin (Bailey, 1946). Such proteins have lent themselves well to *x*-ray studies, since their diffraction patterns can be interpreted in broad outline, though much of the detail is unexplained. Of these proteins, the collagens and keratins serve either as supporting or protective structures, but others like fibrinogen, myosin (the contractile agent in muscle) and tropomyosin, whose properties suggest that it may be a small unit of myosin itself, are more truly functional. We shall consider these latter proteins in relation to their biological function, their structure and amino-acid composition, and attempt an interrelation of these several aspects. All three proteins are of mesodermal origin but, as we shall see, the evidence from structure alone does not suggest a fundamental difference from the proteins of ectodermal origin (hair, fibrils of the epidermis; Rudall, 1946). All possess the characteristic α-pattern, indicative of a regular folding of the polypeptide chain, all are reversibly elastic and can be transformed to the β-form which is characteristic of certain naturally-occurring keratins. There does not appear to be any well-marked histogenic relationship between proteins; collagen, for example, is derived from mesochymal mesoderm but is quite distinct constitutionally from the mesodermal proteins cited above.

2. Soluble Fibrous Proteins

Whilst the fibrous character of keratins, collagens, elastin and reticular tissue is obvious from their mechanical properties, the soluble fibrous proteins are not so easily isolated, and may be more numerous than is generally recognized. Biologists have been aware that anisometric particles may be present in the protoplasm of all cells (Lawrence, Needham & Shen, 1944). Their existence has been inferred largely by optical and other physical methods, but nothing is known of their nature. It has even been suggested that such molecules may arise by the unfolding of corpuscular proteins (Lawrence, Miall, Needham & Shen, 1944). This seems most unlikely, for there is no reason to suppose that anisometric proteins are any less organized than their formulated precursors; fibrinogen and myosin are both sensitive to their environment in respect of physical changes and impairment of biological properties. They must be built by a mechanism just as specific as those presumed to elaborate a corpuscular protein; an extensive unfolding process would tend to a randomness unsuited to Nature's ends. We must thus exercise some caution in interpreting the structure of the keratin, epidermis, myosin, fibrinogen (k-e-m-f) group as something rather simple. That they appear to have a common small-scale intramolecular pattern, which is built up into a grid-structure of side-chain to side-chain and back-bone to back-bone, helps us to a visual interpretation of structure which is lacking for the corpuscular proteins. But it is evident from the results of small-angle diffraction (see Astbury, 1943; Schmitt, Bear, Hall & Jakus, 1946) and electron-microscope studies (Hall, Jakus & Schmitt, 1945), that proteins both of α- and β-type often possess a larger repeating-pattern superimposed upon the smaller which so far has defied exact interpretation. It is as though we saw the small repeating units of a tapestry and not the integrated pattern.

3. Structure of the Keratin-Epidermis-Myosin-Fibrinogen Group

In what follows, we should be sure of what is fact or near-fact, and what is hypothesis, and to what extent our knowledge of fibrous proteins surpasses that of the main body of proteins which we call corpuscular. Firstly, we can differentiate by *x*-ray diffraction those families of proteins which both structurally and otherwise are quite distinct: on the one hand, the collagen group, and on the other, the k-e-m-f group. The distinction between the two is explained and supported by analysis, since the anomaly of the restricted length of the amino-acid residue in collagen could arise from the large numbers of proline, hydroxyproline and glycine residues occurring in the *cis* position in the peptide chain. The k-e-m-f proteins, however, consist predominantly of L-amino-acids with bulky side-chains which can be disposed only in the *trans* configuration.

Secondly, within the k-e-m-f group itself, *x*-ray evidence, supported by elasticity data, distinguishes between the extended proteins of β-type (e.g. feather keratin) and the regularly-folded proteins of α-type. These latter are the more widely distributed, for the β-keratins are largely an evolutionary development in the epidermal structures of reptiles and birds. The α-types can in all cases be transformed to β-types, sometimes by the simple process of stretching, sometimes by more-complex techniques, and this transformation is reversible. The artificial β-keratins do not possess the complex, rich, large-scale pattern found in feather keratin.

Thirdly, the interpretation of the gross structure of α- and β-keratins has been built up from many-sided evidence. The simplest picture that we can conceive for β-keratin is one in which the extended polypeptide chain is juxtaposed with another in the direction of the side-chains to form a sheet or grid; these latter are then built up into a crystallite by piling one sheet on another, the sheets being held together by attractions between the peptide bonds of neighbouring back-bones. The three fundamental spacings of the β-keratin pattern, 3.33A. in the direction of the fibre axis, and 4.65A. and 9.7A. at right-angles to it, are indeed those we would expect for the average amino-acid residue-length, back-bone and side-chain spacing respectively; but further, Astbury, the pioneer in these studies, proved that these last two spacings were at right-angles to each other. There is in addition much chemical evidence, again supported by elastic properties, that the main chains in keratin proper are cross-linked with disulphide bonds arising from cystine residues present in rather large amounts. This again suggests that side-chains of neighbouring polypeptides lie in the same plane.

With regard to α-keratin, the structure proposed is rather more tentative. Assuming that the structure of β-keratin is correct, the problem is to formulate a folding of the grid such that five observed experimental premisses are upheld: (i) the fold is 5.14A. long and must comprise three residues; (ii) the β-form must be approximately twice as long as the α; (iii) the densities of α- and β-forms must be the same; (iv) the integrity of the grid must be preserved on stretching,

i.e. the side-chains must not swing round the main chains but must maintain their general directions; and (v) there must be sufficient room for the side-chains. It seems significant that a simple fold, maintaining (iv), i.e., the folding of the grid in a direction at right-angles to the side-chain direction, can be made to fulfil the other requirements, and to reveal another probable feature—the close-packing of side-chains, which are disposed as triads on either side of the main chain (Astbury, 1941, 1942). In this we see at once a factor which endows the α-form with great stability, since individual groups of each triad might possess strong attractions for each other, as between acid and base, or between paraffinic side-chains. This model of Astbury's cannot be considered final, but as a working hypothesis there seems no reasonable alternative.

In any more-detailed interpretation of the structure of α- and β-keratins, we are on much more uncertain ground, whether it be in the detailed composition of the fold, or in the higher level of molecular organization which concerns the larger repeating units lying at the limit of resolvability by *x*-rays but potentially resolvable by electron-optics. Yet it is clear that, by comparison, what knowledge we have of the fibrous proteins surpasses that for the corpuscular proteins, where only in very recent times has a modest beginning been made in the elucidation of their architectural complexity.

4. Interrelation of the Soluble Fibrous Proteins

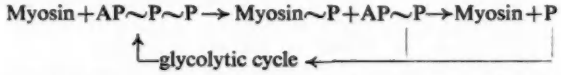
a. General Similarities

When the soluble members of the k-e-m-f group are compared, the similarities revealed by *x*-rays extend to physico-chemical, chemical, and biological properties (Bailey, 1944). Fibrinogen, myosin and tropomyosin all have globulin-like solubility, are salted-out at low ionic strengths, and have similar isoelectric points. When dried by mild methods, the α-pattern is maintained, even where the process involves a loss of solubility or "denaturation". This is an important property and one distinguishing them from the corpuscular proteins, which usually pass to disoriented β-chains on denaturation. There is nothing to suggest that the transformation to the β-form plays any part in the biological role of these proteins. Purified fibrinogen, subjected to the action of thrombin, gives rise to an anastomosis of fibrin filaments which are also of α-type (Bailey *et al.* 1943). In living muscle, the myosin filaments give rise to an α-pattern which, surprisingly enough, is maintained during physiological contraction, where in fact we might expect a transformation indicative of a more folded form (Astbury, 1947). There are compelling reasons to suppose that if physiological contraction does involve an intramolecular folding of chains, this lack of disorientation is more apparent than real. *X*-rays pick out only the crystalline parts of the system, and during moderate contraction the less-crystalline parts will begin to fold first, so that disorientation is delayed. Such an effect is seen in the true keratins.

b. Significant Functional Similarities in Fibrinogen and Myosin

Whatever the detailed mechanism of clotting or of contraction, it seems likely from the nature of the processes that changes in the aggregation of the two proteins are concerned, and this is in keeping with the large numbers of polar groups present. Recently, evidence has been obtained that the action of thrombin on fibrinogen is two-fold, involving the liberation of SH groups and subsequent re-forming of disulphide bridges between adjacent chains (Lyons, 1945). If this is so, it no doubt represents the trigger-mechanism for the aggregation of other side-chains. More important, perhaps, it suggests for fibrin the type of bonding which is accepted for wool and other keratins. These developments are made even more interesting by recent findings on the importance of SH groups in myosin, and their role in an interaction which gives rise structurally to something of the nature of a fibrin clot. To extend the analogy, we must digress to consider some of the properties of myosin.

After the isolation of myosin from the fibril, it soon became apparent from studies of flow-birefringence, elasticity, and *x*-ray diffraction, that the protein possessed all the fibrous properties which might be expected of the ultimate contractile mechanism, and the large amounts present in muscle supported the idea. The energy for contraction must clearly be derived from some reaction capable of building up the potential energy of the polypeptide chains. In point of time, it was known that the break-down of adenosine triphosphate (ATP), a substance containing two labile, energy-rich phosphate groups, was more or less coincidental with contraction, and the subsequent work of Liubimova & Engelhardt (1939) showed that purified myosin itself was capable of splitting ATP. Efforts to separate ATP-ase from myosin have failed, so that the linking of ATP as the direct energy-provider for the intramolecular contractility of the myosin filament seems probable, though the precise mechanism is obscure. The difficulty lies in the fact that the break-down of ATP to adenosine diphosphate and free phosphate cannot contribute to the potential energy of the protein chains, unless in vivo the phosphate is transferred to a protein side-chain or an end-group:



Side by side with the ability to split ATP, myosin in vitro interacts with another remarkable protein-component of the fibril, actin, first isolated by Straub (see Szent-Györgyi, 1945) and intensively studied by the Szeged school. Little is known of the nature of actin. The addition of actin to myosin results in a gelation due to the formation of "actomyosin", which in the electron-microscope is seen to be a highly anastomosed system of protein filaments, reminiscent of the structure of a fibrin clot (Perry & Reed, 1947). In very low concentration, ATP is capable of breaking up the system into its original components, and the viscosity falls. These phenomena cannot satisfactorily be fitted into a scheme of contraction except in a very speculative manner, and it seems wiser at the moment merely to record them. The interesting feature of the reaction, recently shown by Bailey & Perry (1947), is that the viscosity-increase occurs only if the SH groups of myosin are intact; if they are oxidized or substituted, the formation of actomyosin is prevented. Thus there appears to be a co-ordination of the actin with the SH groups of myosin, but on the actin side of the partnership, the groups responsible are unknown; they are not, however, SH or pyrophosphate groups. This SH property links a purely colloidal reaction of myosin with its ATP-ase activity, since this too depends upon the presence

of intact SH groups. Moreover, the extent of inhibition of actomyosin-formation runs parallel with the inhibition of ATP-ase activity as the SH groups are progressively substituted or oxidized (Bailey & Perry, 1947), and it would seem that the same groups are responsible both for enzyme activity and for the colloidal reaction. This receives independent support from the fact that ATP participates in both, and the mechanism of its action could be explained by a competition between actin and ATP for the active enzyme centres. By its ability to prevent actomyosin formation, the affinity of ATP for myosin must be very much greater than that of actin.

In the light of these facts, it is important to record that, in addition to other common properties of fibrinogen and myosin, SH groups play an important, even vital, role in their separate reactions. The importance of SS bonds in the structure of the true keratins needs no emphasis.

c. Possible Relation of Myosin and Tropomyosin

The recently discovered tropomyosin (Bailey, 1946) has been obtained in crystalline form from the skeletal muscle of the rabbit and whiting, and from pig cardiac muscle. It is thus of wide-spread occurrence, and all evidence suggests that it is a component of the fibril and not of the sarcoplasm. Though water-soluble after isolation, it is best obtained from ethanol-ether-dried mince by extraction with strong salt solution, indicating that in situ it forms a complex with some other protein and possibly with lipid. In salt solutions it exists as a homogeneous solute of molecular weight 90,000, but the removal of salt by dialysis results in an enormous increase of viscosity, due to the aggregation of molecules by electrostatic interaction into long fibres (300A. in width and 3000-6000A. long) which exhibit positive flow-birefringence. The ultimate molecule itself is highly asymmetric and composed of either one or two chains in the α-configuration.

The mere fact that tropomyosin is the first protein of α-type to be both crystalline and fibrous renders it of particular interest, quite apart from its possible function in muscle, which as yet is quite unknown. The properties of tropomyosin suggest that it may be a unit from which the myosin chains are in part elaborated. In all its physico-chemical properties, it is the prototype par excellence of myosin itself, and is built on the same intramolecular plan; its method of preparation suggests an intimate connexion with the structural proteins of the fibril. If the role we have suggested for tropomyosin is correct, it is difficult to answer why it exists free at all, except to note that nothing whatever is known of the mechanism of protein synthesis. There is the indirect evidence that in strong urea solutions myosin does in fact depolymerize to units of the size of tropomyosin, a process which affects only the secondary valence forces and not covalent bonds of the polypeptide chain. From a common-sense point of view, it seems almost impossible that a filament of the dimensions of the myosin particle can be rolled off fully-fashioned from its template, but more probable that, as in the transformation of fibrinogen to fibrin, it is built up from smaller units. We have also the example of the interaction of one tropomyosin molecule with another to give a fibrous product and of the further interaction of myosin and actin to give a highly aggregated complex. The supposition, then, that protein fibres are built initially by interaction of fairly large units signifies more than an intuitive belief.

If the analyses of myosin and tropomyosin were identical, the hypothesis would be unshakeable. In actual fact, they are very similar in certain respects: in the high lysine and arginine, and low histidine contents; in the amounts of tyrosine, leucine, valine, proline, methionine, serine, and the very high contents of glutamic acids and identical amounts of aspartic acid. Altogether, both molecules are the most polar (of mixed valency type) that have been encountered. There are differences, however, which leave no doubt that myosin is not built solely from tropomyosin units, even allowing for the fact that a "pure" myosin has not been analyzed. Differences are found in the relative amounts of certain amino-acids and in the absence of tryptophan and glycine from tropomyosin. This is a discouraging aspect in elucidating the relation of the two proteins and complicates, rather than denies, the hypothesis, for it represents but one example of a more general problem.

5. Chemical Make-up of Interrelated Proteins

As we pass from keratin to myosin, it is difficult to see any similarity in chemical composition; in other words, the α-fold can be maintained in spite of chemical differences. Astbury has attempted to explain this fact by assuming that whole groups of amino-acids are important rather than individual amino-acids. In particular, he has suggested that k-e-m-f proteins possess an alternation of polar and non-polar groups along the chain, which, by reference to the α-model, gives rise to an alternation of triads, all polar on one side of the chain, and non-polar on the other (Astbury, 1941, 1942). Such an arrangement would endow the α-form with the elastic properties which in fact it possesses. This formulation cannot strictly be upheld, since it implies that in the k-e-m-f proteins, the polar groups must comprise 50 % of the total; the figures for wool, fibrin, myosin and tropomyosin are 45 %, 54 %, > 57 % and 63 %, respectively.

Here, then, we reach something of an impasse in the finding that the α-fold can exist in spite of, and sometimes by the similarity of, the amino-acid make-up, and other avenues need to be explored. As a general problem, arising from considerations of the stoicheiometry of proteins, Astbury has discussed the possible ways of realizing residue interchange (Astbury, 1943). Either there may be a sequence of certain *types* of residues allotted to definite sites, thus giving rise to a stoicheiometry of types and not of individual residues; or there may be a variable grouping of chains or even of grids of constant composition. The arguments presented in the case of myosin and tropomyosin would favour the latter idea, which also finds support from recent work on corpuscular proteins. There is both physical and chemical evidence that many proteins consist of more than one polypeptide chain. They may depolymerize in urea, in slightly acid or alkaline solutions, in very dilute aqueous solution, and contain α-amino groups capable of chemical reaction and marking the terminal acid of each separate polypeptide chain. In the case of insulin, the sub-molecules of molecular weight 12000 contain 4 peptide chains, one pair of which differs from the remaining pair in end-groups and in amino-acid composition (Sanger, 1945). Is this then the key also to the chemical variations in the k-e-m-f group? If so, it implies that several types of sub-unit are characteristic of the α-proteins, and these are brought together in varying proportion to serve particular ends; it implies too that

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SOME NEWER KNOWLEDGE OF PLASMA PROTEINS

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1 Ultracentrifugal studies
2 Electrophoresis
  a Normal plasmas
  b Pathological plasmas
  c Antisera
3 Bulk fractionation of human plasma-proteins with solvents
4 Clinical application of plasma-fractionation products
References

The past few years have seen such intensive study of the plasma-proteins, and the information accumulated is so extensive, that a short review can indicate only a few salient features. The outburst of activity may be attributed predominantly to the refinement of the technique of electrophoresis, and to the combination of the precise data so obtained with that from physiological, pathological and immunological investigations.

By the early 1930's, a considerable bulk of data relating to the plasma-proteins was available, as a result of studies on "salting-out" and solubility, in conjunction with osmotic pressure and, latterly, ultracentrifugal studies. Before proceeding to the discussion of more recent data, it may be of value to summarize broadly the position at that time.

Three types of protein were distinguished in plasma: fibrinogen, globulin and albumin. It is in this order that these proteins precipitate from plasma as the concentration of neutral salts, such as ammonium sulphate, sodium sulphate or sodium phosphate mixtures, is progressively increased, either by the addition to the plasma of saturated solutions of the salts, or by the direct solution of the solids in the plasma. Inflections in the curves relating the amount of protein precipitated to the concentration of added salt were utilized in attempts to establish the individuality of the components, and also in the development of methods of separating one from another. Two other main variables, pH and temperature, gave added flexibility to the preparative procedures. Similar techniques were used in the examination of the deviations from the normal distribution which were found to occur in pathological conditions, during the course of immunization procedures, and also for the isolation from plasma of protein fractions associated with specific biological activity.

Fibrinogen was sharply distinguished from the other plasma-proteins by its property of forming a fibrin clot as a result of the enzymic activity of thrombin. Albumin had been obtained in crystalline form from some species, and though relatively well defined, was already succumbing to subfractionation. The complexity of the globulin fraction had long been evident. It had been subfractionated into pseudoglobulin, a water-soluble portion, and euglobulin, a portion insoluble in the complete absence of salts, but soluble in dilute salt solutions. The order of molecular weight of these fractions was known, in some cases with a high degree of accuracy as a result of osmotic-pressure determinations.

This, briefly, was the general situation, though an enormous background of detailed information was also available.

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Astbury's limiting or ideal structures (Astbury, 1943) may arise in just this way, with keratin at one extreme of the series, and tropomyosin at the other; it explains also why, in amino-acid composition, myosin and tropomyosin can be so very similar but not identical.

It must be obvious that the attempt to interrelate the k-e-m-f group either biogenetically, biologically or chemically must be very unsatisfactory at this early stage in our knowledge of protein structure. It is equally clear that there does exist a common theme, though all we can see are the variations upon it. The rapid development of amino-acid analysis and its application to the analysis of isolated protein sub-units will be of vital importance to the maintenance or refutation of our current, and perhaps crude, ideas.

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1. ULTRACENTRIFUGAL STUDIES

When a protein solution is subjected to an intense centrifugal field, the molecules sediment at a rate which depends on four factors: the mass of the molecule, the difference of density between the protein and solvent, the viscosity of the solvent, and the centrifugal field strength. The sedimentation velocity in unit field, corrected to standard solvent conditions, is designated the sedimentation constant, and is a characteristic of the molecule.

In the early 1930's, the effectiveness of the analytical ultracentrifuge was widely extended by the introduction of the Lamm-scale method for optical observations, by which the changes in refractive index associated with the boundary of a sedimenting protein could be accurately delineated (Svedberg & Pedersen, 1940). With this improvement it was possible, in addition to measurements of sedimentation constant, to obtain a measure of the homogeneity of the protein under examination. Further, in a mixture of proteins with differing sedimentation constants, an analysis of the quantities of the separate components present could be made, subject to certain reservations.

Using this method it was shown that the proteins of plasma were distributed into two chief groups of differing sedimentation constant. A comparison of the data from whole plasma with that obtained on derived salt-fractionated preparations showed that the sedimenting components corresponded with globulin and albumin, with respective sedimentation constants of about 7.0 and 4.5×10^{-13}.

By combination with the respective values for the diffusion constants, determined by the method developed by Lamm, the following molecular weights were derived, for globulin *c.* 170,000 and for albumin 70,000.

Though the sedimentation and diffusion constants are a function of molecular weight, their precise values are also dependent on the shape of the molecule. Recent measurements indicate that, although the molecular weight of fibrinogen is in the region of 600,000, owing to the elongated form of the molecule its sedimentation constant is so close to the more nearly spherical globulin molecule, that resolution does not occur in the ultracentrifuge. On this account the separate existence of fibrinogen in plasma is not demonstrable by ultracentrifugal studies.

In the plasma of some species small amounts of proteins of very high molecular weight occur, notably in the horse and pig; these appear as separate components in ultracentrifugal analyses and behave as globulins in their solubility relations.

2. ELECTROPHORESIS

In 1937 the initial data obtained with the improved electrophoresis apparatus devised by Tiselius were published (Tiselius, 1937). In addition to providing qualitative information about the number of components present in complex protein solutions, and precise values of their respective mobilities, the apparatus was adapted to the isolation of electrophoretically-homogeneous proteins in small quantities from mixtures.

The original simple "Schlieren" optical system used with the apparatus, though capable of indicating the presence of several components, gave no measure of the quantities in which they occurred. The Lamm-scale method was used to a limited extent, but owing to its laborious nature it was quickly superseded by other methods, notably the "Schlieren scanning" and "diagonal Schlieren" systems, each of which provides quantitative data (Abramson, Moyer & Gorin, 1942).

The migration of a dissolved protein in an electric field is primarily determined by the net charge of the molecule, and since this is predominantly derived from the ionization of basic and acidic groups, it is in its turn a function of the pH and salt-content of the medium in which the protein is dissolved. Electrophoretic phenomena are therefore more closely related to the chemical structure of the molecule than sedimentation, which depends chiefly on size and shape.

From a mixture of proteins an electrophoresis-pattern is obtained in which each component gives rise, as in the ultracentrifuge, to a separate peak, closely allied to a normal distribution curve. This is subject to the migration having continued for a sufficient period under suitable conditions.

a. Normal Plasmas

In his original examination of horse serum at pH 8, Tiselius (1937) distinguished four components. That with the highest mobility was identified as albumin, the remaining three as globulin, and designated α, β and γ in descending order of mobility. The more recent examination of human plasma indicates that six components are present: albumin, α-globulin which, under special conditions, splits into α_1 and α_2, β-globulin, fibrinogen and γ-globulin in order of mobility (Longsworth, 1942).

The quantitative constitution of normal human plasma determined by electrophoretic analysis, in which each component is given as a percentage of the total protein, is as follows (Edsall, 1947):—albumin 55; globulin α 14; β 13.5; γ 11; fibrinogen 6.5. These proportions remain remarkably constant in the normal individual, as the agreement between determinations in laboratories in many countries has shown.

The plasma of other species shows qualitative and quantitative electrophoretic deviations from normal human plasma with respect to the number, amount and mobility of the components. For example, in the horse the β-globulin is represented by two components β_1 and β_2, and in the dog the pattern appears to be even more complex.

It may be of interest to point out the relation of the pseudo- and euglobulin fractions to the electrophoretic components. Both of these are mixtures; in pseudoglobulin the α- and β-globulins predominate, whilst in euglobulin the chief constituents are β- and γ-globulins.

In human plasma, most of the protein-bound lipoid is associated with the α- and β-globulins. The albumin does not appear to have any carbohydrate attached to it, and in this respect differs from horse-serum albumin.

Although the plasma-components revealed by electrophoresis display a reasonable degree of electrochemical homogeneity, it is important to appreciate that this does not imply absolute chemical or physiological homogeneity. The wide range of physiologically- and immunologically-active proteins detectable in plasma is apposite to this point, and also the fact that the electrophoretically-homogeneous components are susceptible to further fractionation by solubility-methods. Further, the activity of proteins associated with specific biological effects is frequently so high in relation to mass, that the quantities present in plasma may

be far below the power of resolution of the electrophoresis-apparatus.

b. Pathological Plasmas

The plasma and serum from a large number of pathological conditions have been subjected to electrophoretic analysis and already a considerable literature exists. To discuss the findings related to specific diseases would require detail beyond the scope of this article. In general, the quantitative distribution of the components has frequently been found to diverge, sometimes very markedly, from the normal. It appears to be exceptional for an entirely new component to appear in such plasmas.

In febrile conditions the proportion of α-globulin is usually enhanced, whereas in nephrosis the albumin content is very low and the β-globulin is increased to a remarkable extent. Several conditions are associated with increases in the γ-globulin, notably cirrhosis of the liver and multiple myelomatosis, though in the latter abnormally high β-globulin contents may be found (Abramson *et al.* 1942). In infectious conditions there is also a tendency for the γ-globulin to be increased which is consistent with the finding that many antibodies are associated with this component.

This brief summary discloses that the changes occurring in the plasma-protein distribution in pathological conditions are not specifically related to any one disease. It is possible that the correlation of the clinical course of various diseases with alterations in the electrophoretic patterns may prove valuable in the assessment of therapeutic measures.

c. Antisera

In the production of therapeutic antisera, the horse is most generally utilized. In this animal the antibacterial antibodies appear to be associated with γ-globulin which in hyperimmune serum is often very much increased in amount. In antitoxic sera the occurrence of two antibodies has been demonstrated, one associated with the β-, the other with γ-globulin, and also differing from one another in certain biological characteristics. In the rabbit, antibodies appear usually in the γ-globulin (Abramson *et al.* 1942).

3. BULK FRACTIONATION OF HUMAN PLASMA-PROTEINS WITH SOLVENTS

Although, as already mentioned, it is possible to isolate the individual proteins from human plasma by electrophoresis, the scale on which this can be accomplished is very limited, and from this point of view the method is useful only on a research basis. In conjunction with bulk-fractionation methods, the apparatus has proved of inestimable value in providing an independent means of controlling and assessing improvements in the resolution of fractionation-procedures.

The separation of proteins has generally been carried out in very concentrated salt solutions, in the region of 2–3 molar, a procedure which has two main disadvantages. Firstly, high salt-concentrations mask specific salt-protein effects which may be utilized in improving the resolution of separations. Secondly, the products must be freed from the precipitating salt by dialysis, a procedure difficult to carry out under the aseptic conditions desirable if the product is required for clinical purposes.

In attempting to separate proteins in a relatively pure condition from a mixture in aqueous solution, there are several variables which can be used to establish conditions such that a desired protein can be caused to precipitate more or less completely, leaving others in solution. The following are the determinant variables: pH, salt concentration, temperature, total protein concentration—and, as a result of recent studies, solvent concentration.

If a solvent is used to reduce the solubility of a protein, the electrolyte-content of the system can be maintained in as low a concentration-range as may be necessary. It is simpler to maintain aseptic precautions when adding solvents: indeed those solvents suitable for precipitation purposes tend to be bacteriostatic. Finally, the solvents can be removed from the products by freeze-drying, an operation easily performed under sterile conditions. The one disadvantage of solvents lies in their tendency to cause denaturation and loss of biological activity in proteins at room-temperature, and their use necessitates processing at temperatures ranging from 0° to −10° C. The precise examination of such methods has largely been due to E. J. Cohn and his associates, though sporadic papers have appeared in the literature as far back as 1908 (Cohn *et al.* 1946).

Such investigations were stimulated by the urgent needs of war and were initially directed towards the production of a stable liquid transfusion-material. This presents certain advantages over freeze-dried plasma, although under proper conditions the latter retains its properties for an indefinite period. Normal human citrate-plasma on storage tends to clot, and even if the fibrinogen is removed, precipitates form which simulate bacterial infection. These precipitates derive from the breakdown of complexes formed by lipoids with the plasma-globulins. In the production of a stable liquid transfusion-material from human plasma, two methods of attack are possible. The fibrinogen and globulins may be removed entirely, providing a stable solution of albumin. Alternatively, the fibrinogen and unstable lipoids may be removed from the plasma and the whole of the remaining proteins made available. The former method was followed in the USA, and in Britain the latter was explored.

The system of fractionation of human plasma with ethanol at low temperature developed by E. J. Cohn and his colleagues (Cohn *et al.* 1946) was primarily aimed at the preparation of pure human serum-albumin for transfusion. As the work progressed, a secondary objective developed: to separate the plasma-proteins into a limited number of main fractions corresponding as closely as possible to the individual electrophoretic components. These main fractions then provided the basis of various subfractionations, oriented with reference to specific biological activities. The following purified materials were made available in quantities and at concentrations adequate for clinical purposes: albumin, fibrinogen, thrombin, γ-globulin and erythrocyte isoagglutinins.

By the use of ether in the fractionation of human plasma, fibrinogen, thrombin, globulin concentrates and a stable delipoided transfusion-fluid have been made available in Great Britain (Kekwick, Record & Mackay, 1946).

4. CLINICAL APPLICATION OF PLASMA-FRACTIONATION PRODUCTS

Perhaps the most versatile of the products of plasma fractionation are fibrinogen and thrombin (Bailey & Ingraham, 1944). Since the clotting-time of fibrinogen-thrombin solutions can be accurately controlled, a liquid mixture, which subsequently clots, can be applied locally. The tensile strength of fibrin clots, though also a function of other variables, increases with fibrinogen concentration, and solutions of fibrinogen up to ten times (2%) the corresponding concentration in plasma are readily attainable. The clots formed from such solutions have been used to suture severed nerves by a process of "soldering". Rather lower concentrations of fibrinogen provide, with thrombin, an excellent adhesive for the application and fixing of skin grafts, dispensing with the necessity for pressure dressings. Grafts fixed in this manner vascularize with extraordinary rapidity, and the tendency to bronze pigmentation appears to be reduced.

Fibrin films, resembling sheet cellophan in appearance, have been successfully used as dural substitute with marked absence of adhesion. The film is eventually replaced by fresh dural growth.

Somewhat less purified fibrinogen solutions are utilized in the production of fibrin foam. By suitable devices, these solutions are beaten to a finely dispersed foam which is "set" by adding thrombin and then dried from the frozen state. Such foams if rewetted tend to shrink rapidly, but this can be prevented by baking the dried foam at 130° to 170° C. The dried foam will absorb almost its own volume of thrombin solution, and is used in conjunction with this for local haemostasis in internal surgery. The foam is allowed to remain in situ following operative procedures, and eventually becomes organized into the tissue without scar-formation.

It has been established that the antibodies in many infectious diseases are associated with the γ-globulin of normal adult plasma (Enders, 1944; Stokes, Maris & Gellis, 1944; Ordmann, Jennings & Janeway, 1944). Concentrates of this protein containing 15 g. protein/100 ml. have been very successfully used in the control of measles, and may be useful in infectious hepatitis. For measles, intramuscular injections up to 5 ml. are required. The use of similar concentrates prepared from convalescent-plasma pools from other infectious diseases, for example, mumps, has been examined.

The A and B isohaemagglutinins, which appear to be associated with β-globulin, have been purified and concentrated from pools of plasma of suitable blood-group. High-titre sera are required for accurate blood-group testing, and concentration methods make available the agglutinins from plasmas whose titre initially is too low.

Purified albumin solutions containing 25 g./100 ml. have been satisfactory for transfusion in cases of shock and hypoproteinaemic oedema.

Further research may indicate the clinical usefulness of other fractions derived from human plasma.

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AMINO-ACIDS IN NUTRITION

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1 Endogenous and exogenous metabolism of protein
2 Protein storage
3 Regulation of protein metabolism
4 Clinical symptoms of specific amino-acid deficiencies
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Protein metabolism in general has been fully discussed in this journal in 1944 by Cuthbertson[1], and the effect of protein on convalescence, recovery from injuries and burns has been considered by Peters[2] (1945) and Cuthbertson[3] (1945) respectively. It is not the purpose of this essay to bring these reviews up to date, but rather to consider some general problems of protein metabolism, to indicate gaps in our knowledge and to discuss possible future lines of work.

1. Endogenous and Exogenous Metabolism of Protein

Those early workers, such as Liebig, Boussingault, Voit and Pettenkofer, who introduced exact methods into the field of protein metabolism, were greatly impressed by the fact that the adult mammalian organism tends to keep its protein-content constant under the most diverse dietary conditions. Thus, a large increase of protein-intake leads after a very short lag to a corresponding rise in urinary N excretion, whilst starvation or a specific protein-deficiency produces a very marked reduction in N output. We know now that a similar regulation occurs in the metabolism of water and electrolytes. Voit (1866) suggested as an explanation that the protein molecules which form part of the living structure were metabolically almost inert, whilst the "storage protein" which was derived from the nitrogen present in the diet and which was assumed to circulate freely in the tissue-fluids was readily catabolized. This theory was further elaborated in a later publication (Voit, 1881) and has dominated reasoning in this field up to the last decade. Voit did not make it clear whether the differences which were supposed to exist between "tissue protein" and "circulating protein" were of a chemical or physical nature. He admitted that there may be an interchange between these two classes of protein, but emphasized that such reactions must be very slow. Rubner, who contributed a large amount of experimental work and a possibly disproportionate volume of speculative writing to the development of this field, investigated N excretion in subjects supplied with their full caloric requirements but lacking protein completely. The constant and small N output observed under these conditions was ascribed to the slow rate of metabolism of the "living" or "tissue-protein". This "wear and tear" quota was assumed to be independent of dietary changes (Rubner, 1908; 1911).

The next important step in the development of this theory was taken by Folin (1905). This author compared changes in the composition of urine with the level of protein in the diet, and found that, whilst the concentration of some constituents such as urea was proportional to N intake, the excretion of other substances like creatinine was not influenced by variations in the diet. Folin suggested that the concentration of substances of the second group is a measure of the "endogenous" metabolism of the "tissue proteins" of Voit and is related to the "wear and tear" quota of Rubner. Excretion of urea and sulphate on the other hand corresponds mainly, but not exclusively, to the breakdown of excess dietary protein, and is related to "exogenous" metabolism. Thus Folin's extension of Voit's fundamental concept consisted mainly in relating the two branches of protein metabolism to certain nitrogenous substances in urine. However, Folin differed from Voit in one important point—he believed that the dietary protein is hydrolyzed to amino-acids and that these compounds of low molecular weight are mainly directly oxidized, without being first incorporated into "circulating protein".

Although the Voit-Folin theory was almost universally accepted, there have been a few dissentient voices. Thus Pflüger (1893) maintained that protein after absorption becomes quickly incorporated into the cell-structure and partakes in the general metabolic reactions of the organism. Much later Borsook & Keighley (1935) stated their belief that the sharp distinction between endogenous and exogenous metabolism was unjustified. However, the experimental evidence produced was not convincing, and it was only when isotopes were introduced into protein biochemistry by Schoenheimer, that the classical concepts had to be revised (for reviews see Schoenheimer & Rittenberg, 1940; Schoenheimer, 1946). Schoenheimer, Rittenberg and their colleagues used N^{15} to mark the amino-acids or ammonium salts introduced in the diet, and followed the fate of the nitrogen atom in the organism. It was found that only a fraction of the labelled element was excreted in the urine; most of the nitrogen was found in the tissues. In fact, it may be inferred that all cells, even those of connective tissue and muscle, which had been thought to be particularly inert, are in a state of dynamic equilibrium with the nitrogenous compounds supplied in the diet.

Thus the old idea of Voit that the "tissue protein" is inert, and the modified theories of Rubner and Folin which assume that the protein turn-over of the body-substance is represented by the N excretion on a protein-free diet, are equally incorrect. Instead, we have to assume that the catabolic and anabolic reactions take place at a great speed and are fairly well balanced. Urinary N represents, therefore, only a small difference between the amounts of protein broken down and synthesized every day. However, the experimental facts on which the old theories were based need to be reconsidered, and it can be shown that the terms "endogenous" and "exogenous" metabolism can still be usefully employed, provided that their definition is adjusted to modern requirements.

In the old concept of Voit and Folin it was assumed that the terms endogenous and exogenous represented physical

[1] [*BMB* 486] [2] [*BMB* 688] [3] [*BMB* 691]

realities, i.e., the expressions were used to describe the actual fate of a metabolite in the body. Such an interpretation is now untenable, but the terms can still be used to describe items on a balance-sheet. Endogenous nitrogen has an exact physical meaning, if applied, for example, to the excretion of nitrogen on a protein-free diet, but if used in calculations of nutritional efficiency with protein-containing diets it represents, in general, nothing but a convenient fiction of nutritional accountancy. In certain cases a more precise meaning can be attached to the old terms. The excretion of creatinine in the urine is remarkably constant for any one individual in the absence of disease and is not markedly influenced by changes in the diet. The urinary creatinine is formed from the creatine-phosphate which is present mainly in muscle. Creatine in its turn is produced from arginine, glycine and methyl-donors, which all occur in the diet. Thus, the ultimate source of the carbon and nitrogen of creatinine, like that of urea and amino-acids, is largely exogenous. The difference between the two classes of compounds lies not so much in the nature of the different reactions involved, but in their rates. Creatine is formed in the body and creatinine is excreted in the urine at rates little influenced by the supply of precursors. Moreover, all the various reactions appear to be irreversible. The urinary creatinine may thus be endogenous in the sense that the amount formed is proportional to the mass of muscular tissue and is not related to the N content of the diet.

A somewhat similar position may exist with proteins. Schoenheimer & Rittenberg (1940) have shown that different organs vary greatly with respect to rate of N exchange. Further work is likely to show that different proteins, even in the same organ, are not metabolically active to the same extent. Thus, there will be some species of proteins which have a very high turn-over rate and correspond to the "circulating" protein of Voit. The same proteins may also increase in amount, if the intake of nitrogen is raised. Other types of protein molecules may be relatively inert and not quickly responsive to changes of diet. Such substances would represent the "tissue-protein" of Voit. Thus, these old terms may be used to describe not so much sharp qualitative differences between proteins, but quantitative variations in the rates of N exchange which are susceptible to unknown regulating factors. How far such differences are reflected in the chemical structures of the different proteins, only further research can show.

The use of labelled elements has not yet solved, but only shifted, the classical problems of protein metabolism. Are the rates of catabolic and anabolic reactions influenced by starvation, the N level in the diet, hormones, or specifically by some amino-acids? And above all, by what mechanism is the protein content of the body kept constant within fairly narrow limits in spite of the large changes taking place in the tissues? These are problems which can be tackled only with the aid of labelled elements.

2. Protein Storage

The assumption which has been made in the preceding section, that the N content of the adult organism tends to remain constant, is not wholly correct. It has been shown for man that superimposition of extra protein on a diet adequate for maintenance of body-weight and N equilibrium leads to marked retention of N (Cuthbertson, McCutcheon & Munro, 1937), and a similar result was produced by feeding carbohydrate (Cuthbertson & Munro, 1937). The storage of protein in the adult animal has recently been reviewed by Kosterlitz & Campbell (1945) who have themselves made important original contributions to our knowledge in this field. They have found that a fraction of liver-cytoplasm comprising protein, ribonucleic acid and phospholipin is quickly lost on reduction of protein below a certain level, or somewhat less readily by caloric restriction. This labile liver-cytoplasm is quickly regained if the protein intake is again raised above minimum requirements. Similar changes in other organs may occur, but they have been less carefully investigated. Another approach to the problem of protein storage has been made by Munro & Chalmers (1945). The work of Cuthbertson had shown that after injury, both in man and laboratory animals, there is an increase in the excretion of nitrogenous substances in the urine. This excessive excretion is reduced if the protein content of the diet is decreased, and becomes very small and transient on a protein-free diet. It thus appears that the well-fed organism has certain labile protein-reserves which are readily lost on injury. The amount of N lost is too large to be entirely accounted for by the labile liver-cytoplasm. The location of this reserve is unknown and it is also uncertain whether both this fraction and the labile liver-fraction differ chemically from the ordinary protein components of cell-cytoplasm. It is quite likely that they are again only items on a balance-sheet, and that their accumulation and mobilization are regulated by some unknown mechanism which is very sensitive to changes in the dietary intake of calories and protein.

The amounts of amino-acids and peptides present as such in tissues are small and are, quantitatively at least, unimportant as far as N storage is concerned. However, relatively large amounts of the tripeptide, glutathione, are present in all organs, but especially in the liver. The concentration of this peptide in the liver can be influenced within very wide limits by the composition of the diet (Leaf & Neuberger, 1947), and especially by its content of cystine and methionine.

3. Regulation of Protein Metabolism

The dynamic state of the body-constituents, as revealed by the isotope method, implies that oxidative, reductive and other reactions associated with large changes of free energy occur at a rate much greater than is indicated by the over-all energy-requirements of the organism or by the actual amounts of end-products excreted in the expiratory air and in the urine. It follows that reactions leading to a loss of free energy are coupled with those in which a net gain of free energy is produced. The question therefore arises as to how the relative constancy of basal metabolism, basal N execretion and N balance of the adult organism is ensured. It is at present impossible to answer these questions satisfactorily. It can be assumed that factors such as oxygen-tension, cellular concentrations of the various enzymes and coenzymes, and also those of the free amino-acids, influence the rates of the different catabolic and anabolic reactions which constitute protein metabolism. But there is evidence that, apart from these local cellular factors, hormones

may affect directly or indirectly the rate of reactions in which amino-acids take part.

It has been known for a long time that administration of thyroid increases N excretion. This effect may possibly not be specific but may result from the general stimulation of tissue oxidation. It is known that the "endogenous" N excretion is proportional to the basal metabolism, which is raised in hyperthyroidism. Recent american work has shown that androgens, especially testosterone, produce N retention in castrates, and similar results have been claimed for oestrogens. Moreover, both catabolic and anabolic effects on protein metabolism have been produced by the various steroids found in the adrenal cortex. Nothing is known about the way in which these substances act. One possibility is that at least some of these steroids, i.e., those lacking a hydroxyl group in position 11, act not directly on protein metabolism but indirectly through their effect on the excretion of sodium and potassium. Recent work of Hastings and others (see e.g. Hastings & Buchanan, 1942) has shown that various enzyme-reactions are greatly influenced by the ionic composition of the medium. It is thus quite likely that the rate of protein synthesis is affected by the concentration of sodium and potassium, respectively, and any hormone which regulates the excretion of these cations by the kidney may have an indirect influence on protein metabolism. The other group of biologically-active steroids of the adrenal cortex may affect protein metabolism through their action on carbohydrate oxidation.

More is known about the relationship between the pituitary and N excretion. It has been known for some time that the growth-hormone stimulates N retention. Part of this effect is undoubtedly due to the increased appetite which results from the administration of this hormone. But it has been shown in paired-feeding experiments, in which the controls received a diet of caloric value equal to that given to the animals injected with pituitary extracts, that increased growth occurs even under conditions of caloric restriction (Lee & Schaffer, 1934). Recent work by Young (1945) has fully confirmed these results; it was demonstrated that administration of pituitary extract to various animals, kept on diets which under normal conditions were just sufficient to maintain body-weight, produced N retention and, in the cat and dog, diabetes. The caloric requirements of these animals were largely covered by the combustion of fat, and this enabled the animal to retain N in spite of caloric restriction. Young suggests that this action on N balance is associated with the diabetogenic activity of these extracts. This may mean that the pituitary influences growth largely through its effect on carbohydrate oxidation. Some information is available which suggests that insulin enhances N retention, but further work on this point is required before the mechanism can be considered fully established.

The protein-sparing action of carbohydrate has been known for some time, and it has been generally assumed that this resulted from a purely energetic replacement of protein by carbohydrate. In other words the combustion of carbohydrate released a calorically-equivalent amount of protein for purposes of growth and tissue-regeneration. But there is an alternative explanation. Various reversible and irreversible reactions in which amino-acids are concerned produce α-keto-acids, many of which are associated with the metabolism of carbohydrates. Indeed, the keto-acids which correspond to those amino-acids which, according to isotope experiments, show the fastest turnover-rate—such as aspartic and glutamic acid—are most closely linked with the oxidation of glucose. It is thus possible that the protein-sparing action of carbohydrate may be due to the fact that glucose provides precursors of non-essential amino-acids, and that ammonia is then utilized for amino-acid synthesis instead of being converted into urea. In the absence of insulin, oxidation of glucose is inhibited, and the ammonia liberated in intermediary reactions is lost for purposes of protein formation.

4. Clinical Symptoms of Specific Amino-acid Deficiencies

The essential amino-acids, i.e., those nitrogenous compounds which the mammalian organism cannot synthesize from substances normally present in the diet, have often been compared to vitamins. There are, however, important biological differences between these two groups of essential metabolites. Although complex interrelationships exist between certain vitamins, in general the requirements for various vitamins are largely independent of each other and additive. Moreover, many vitamins can be stored as such in the body. On the other hand, the formation of protein can proceed only if all the essential amino-acids are provided in the diet; single amino-acids can be stored only in insignificant quantities. It is therefore not surprising that, apart from exceptions to be discussed below, deficiencies of single amino-acids produce a clinical picture which is not specific for any one compound. What is generally observed is cessation of growth, loss of weight, hypoproteinaemia and a relatively mild anaemia. The animals get adapted, to some extent, to the lack of protein by reduction of N output to a minimum and by losing protein first from the non-essential organs. Such animals appear to be less resistant to infection, possibly due to interference with antibody production.

The position of the sulphur-containing amino-acids, methionine and cystine, appears to differ from that of other essential amino-acids. Methionine is, apart from being building-material of proteins, a donor of methyl-groups for the synthesis of choline and other substances. Cystine is a precursor of glutathione, of taurine and possibly other compounds of low molecular weight. It is therefore not surprising that a deficiency of these amino-acids produces more-specific clinical symptoms. With young rats, feeding of amino-acid mixtures lacking these sulphur-containing compounds produced an acute hepatic necrosis which could be prevented by the addition of either cystine or methionine (Glynn, Himsworth & Neuberger, 1945). However, later work has indicated that it is necessary for the production of necrosis to remove from the diet, not only these two amino-acids, but also tocopherol. The exact mechanism of the causation of these liver lesions is therefore still obscure.

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DR. ERNEST BALDWIN is a University Lecturer in the Cambridge School of Biochemistry. He was educated at St. John's College, Cambridge, where he held a Fellowship from 1936 to 1941. He is a member of the Marine Biological Association of the United Kingdom, of the Biochemical Society, of the Society for Experimental Biology and of the Cambridge Philosophical Society. He has worked mainly on comparative biochemistry, especially on muscle, electric tissue, and the nitrogenous metabolism of invertebrates. During the war he was engaged in research on anthelmintics. He has played a leading part in developing the teaching of pure biochemistry to undergraduate science students at Cambridge and is the author of two textbooks: *An introduction to comparative biochemistry* (Cambridge University Press, 2nd ed., 1940) and *Dynamic aspects of biochemistry* (Cambridge University Press, 1947).

DR. MARJORY STEPHENSON is director of the Medical Research Council's Unit for Chemical Microbiology in Cambridge. Dr. Stephenson, who is a Fellow of the Royal Society, has worked for many years on problems of bacterial enzyme chemistry and is the author of *Bacterial metabolism*, the well-known textbook on the subject, as well as of a series of papers published mainly in the *Biochemical Journal*. The main trend of her work has been the study of bacterial enzymes, with a view to elucidating problems of growth and adaptation. She has recently been appointed Reader in Microbiological Chemistry in the University of Cambridge.

DR. E. F. GALE is a member of the scientific staff of the Medical Research Council and has worked in the Council's Unit for Chemical Microbiology at Cambridge for some years on the amino-acid metabolism of bacteria. He worked out the conditions necessary for the production of amines by bacteria and (with Epps) first obtained the amino-acid decarboxylases in a cell-free state; these investigations eventually led to the identification of pyridoxal phosphate as the prosthetic group of these enzymes. He is now studying the assimilation of amino-acids by bacteria and the effect of chemotherapeutic agents, particularly penicillin, on the processes involved. Publications: "Bacterial amino-acid decarboxylases" (*Advances in Enzymology*, 1946, **6**, 1); *The chemical activities of bacteria* (University Tutorial Press, 1947); papers in *Biochemical Journal* and *Journal of General Microbiology*, etc.

DR. D. D. WOODS read biochemistry at Cambridge and worked there for a number of years on problems of bacterial metabolism in Dr. M. Stephenson's unit. For part of this period he held a Beit Memorial Fellowship. In 1939 he joined the Medical Research Council Unit for Bacterial Chemistry (under Sir Paul Fildes) and in 1940 published his observations on the relation of *p*-aminobenzoic acid to the mode of action of the sulphonamides (*Brit. J. exp. Path.* 1940, **21**, 74) which were the basis of an hypothesis concerning the fundamental biochemical action of these drugs which is now widely accepted. For the greater part of the war Dr. Woods was on the staff of the Microbiological Research Department, Porton. He is now Reader in Microbiology in the Department of Biochemistry, University of Oxford and is continuing his work on the biochemical aspects of sulphonamide action and related subjects. Dr. Woods is on the editorial staff of the *British Journal of Experimental Pathology* and the *Journal of General Microbiology*.

PROFESSOR R. A. PETERS has previously contributed to the Bulletin a paper on "The biochemical lesion in thermal burns" (*BMB* 688), with which a note on his work was published.

PROFESSOR R. H. S. THOMPSON was educated at Trinity College, Oxford, and Guy's Hospital Medical School. Holding the Adrian Stokes Travelling Fellowship, he worked from 1937 to 1938 in the Hospital of the Rockefeller Institute for Medical Research, New York. In 1938 he was awarded the Gillson Research Scholarship in Pathology by the Society of Apothecaries of London. Since 1938 he has been a Medical Fellow of University College, Oxford and Demonstrator in Biochemistry, Oxford. From 1939 to 1944 Professor Thompson was a member of the Extra-mural Research Team, Chemical Defence Research Department, Ministry of Supply, under the direction of Professor R. A. Peters, who also contributes a paper to this number (*BMB* 1198); and from 1944 to 1946 served as Major, RAMC, attached to the Australian Army. In 1946 he became Dean of the Medical School, Oxford University, and in October 1947 was appointed to the Chair of Chemical Pathology at Guy's Hospital Medical School, London. He is also Secretary of the Medical Research Council Conference on British Anti-Lewisite. Professor Thompson has worked with Professor Peters on pyruvate metabolism in vitamin-B_1 deficiency, and with Dr. R. J. Dubos on the nucleic acids of pneumococci. He has done much work on various applications of BAL, and on the action on cholinesterases of certain substances of interest in chemical warfare.

MR. M. V. TRACEY is a member of the biochemistry department of Rothamsted Experimental Station. He graduated from Cambridge University in 1940, where he had read biochemistry under Gowland Hopkins. After work on the manufacture and development of propellants for the Admiralty and on blood transfusion for the Ministry of Health he went to Rothamsted and worked on the proteases of green leaves. He is the author of a book on proteins at present in press.

MR. N. W. PIRIE studied under Hopkins in Cambridge; his first research there was on the chemistry and metabolism of sulphur compounds. Opportunities of collaboration with animal and plant pathologists in Cambridge led to research on antigens from *Brucella* and on plant viruses. This led to a general interest in large molecules of various types and to a tendency to doubt the usefulness of many of the concepts used in describing them. The biochemical department at Rothamsted, of which Pirie is head, is concerned with the isolation and characterization of the colloidal components of normal and virus-infected leaves. From this it is hoped that some understanding of the state of viruses in the cell and of their mode of multiplication will be gained.

PROFESSOR A. WORMALL is professor of biochemistry and chemistry in the University of London, at St. Bartholomew's Hospital Medical College. He graduated with honours in chemistry at Leeds in 1921, and was awarded his D.Sc. in 1930. He was demonstrator, and later lecturer, in biochemistry in the department of physiology at Leeds up to his appointment to the Chair at St. Bartholomew's in 1936. In 1928 he was awarded a Rockefeller Medical Fellowship by the Medical Research Council, and he spent a year with Landsteiner at the Rockefeller Institute studying some chemical problems of immunity. At the request of the Colonial Office he went to Uganda in 1930 to carry out investigations on human trypanosomiasis. These investigations were mainly concerned with the carbohydrate metabolism of sleeping-sickness patients, and with diagnostic tests for the disease; in particular, the red-cell adhesion test was suitably modified and found to be of definite practical value. Professor Wormall is specially interested in the chemistry of immunity, and in more recent years he has been using radioactive and stable isotopes for these studies. During the recent war, however, much of this work had to be put on one side in favour of more urgent mustard-gas problems. This mustard-gas work, started early in 1939, was later continued by a team under the leadership of

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AMINO-ACIDS IN NUTRITION

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Glynn, L. E., Himsworth, H. P. & Neuberger, A. (1945) *Brit. J. exp. Path.* **26**, 326
Hastings, A. B. & Buchanan, J. M. (1942) *Proc. nat. Acad. Sci., Wash.* **28**, 478
Kosterlitz, H. W. & Campbell, R. M. (1945) *Nutr. Abstr. Rev.* **15**, 1
Leaf, G. & Neuberger, A. (1947) *Biochem. J.* **41**, 280
Lee, M. O. & Schaffer, N. K. (1934) *J. Nutrit.* **7**, 337
Munro, H. N. & Chalmers, M. I. (1945) *Brit. J. exp. Path.* **26**, 396
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Rubner, M. (1908) *Arch. Hyg., Berl.* **66**, 1
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Schoenheimer, R. (1946) *The dynamic state of body constituents*, Cambridge
Schoenheimer, R. & Rittenberg, D. (1940) *Physiol. Rev.* **20**, 218
Voit, C. (1866) *Z. Biol.* **2**, 307
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Young, F. G. (1945) *Biochem. J.* **39**, 515

Professor Wormall as an extramural war investigation for the Ministry of Supply. In much of this work radioactive sulphur was used, and radioactive isotopic tracers are now being used in his laboratory for the study of immunochemistry and some general problems of biochemistry.

DR. KENNETH BAILEY is an authority on proteins and is particularly concerned with structural proteins connected with the contractility of muscle. He graduated at Birmingham and after three years of research on carbohydrates took up the study of proteins at Imperial College and later at Cambridge. In 1939 he was awarded a Rockefeller Fellowship to study physico-chemical aspects of proteins under Dr. E. J. Cohn of the Harvard Medical School. At present he holds an Imperial Chemical Industries Research Fellowship. His early work in collaboration with Professor W. T. Astbury led to a general formulation of the mechanism of denaturation and was applied to the large-scale production of artificial wools. Later, he worked on the chemical and enzyme properties of myosin and on the nature of fibrinogen-fibrin and has recently elucidated the myosin-actin interaction. In addition, he has isolated a new crystalline, fibrous protein, tropomyosin, from the muscle fibril, and has also taken part in the preparation of pure yeast pyrophosphatase and crystalline hexokinase. Publications include two reviews on muscle proteins (*Recent Advances in Protein Chemistry*, 1944, **1**, 289; *Annu. Rep. Chem. Soc.*, 1946, **43**, 280).

DR. R. A. KEKWICK is director of the Division of Biophysics at the Lister Institute, London, and collaborates with the Medical Research Council Blood Products Unit, which is also housed at the Lister Institute, in the preparation of human plasma products. His interests have always been associated with the physico-chemical aspects of protein behaviour, with special reference to ultracentrifuge and electrophoresis measurements and their correlation with specific biological activity. His studies have ranged over pathological human sera, therapeutic antitoxic sera, and the design of bulk protein fractionation procedures. Papers have appeared in the *Biochemical Journal* and the *British Journal of Experimental Pathology*.

DR. A. NEUBERGER is a member of the Scientific Staff of the Medical Research Council at the National Institute for Medical Research. He is Secretary of the Protein Requirements Committee of the MRC and a member of the Committee of Protein Requirements of Infants; he is also a member of the editorial board of the *Biochemical Journal*. Dr. Neuberger was awarded the William Julius Mickle Fellowship of the University of London for 1946–47. His research up to the war was concerned mainly with the structural chemistry of proteins, dissociation constants of amino-acids and chemistry of amino-sugars. Since the war he has become interested in the metabolism of amino-acids and problems of protein nutrition. Various papers by Dr. Neuberger have been published in the *Biochemical Journal*, *Journal of the Chemical Society*, and *Proceedings of the Royal Society*.

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BRITISH MEDICAL BULLETIN
VOLUME 5 · NUMBER 4-5 · 1948

PART TWO · COMMENTARY
HISTORY · DOCUMENTATION

IN previous volumes the Bulletin contained, in addition to the scientific symposium which occupied the greater part of each number, subsidiary sections of bibliographical and historical interest. Starting with the first number of Volume 5, the Bulletin has been clearly divided into two parts. The collective monograph on a special subject which had become the characteristic feature of the Bulletin now constitutes Part I. Part II contains miscellaneous articles on medical subjects of scientific, bibliographical, and historical interest. The book-review section is extended and there are, as before, sections devoted to historical notes, film-reviews, and lists of contents of current british medical and cognate periodicals. It is our intention that Part II should be a medium for extending the range of interest of each number of the Bulletin and for enhancing its continuity as a periodical.

THE MEDICAL RESEARCH COUNCIL
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BRITISH BIOCHEMISTRY ... ... *A. R. Trim*
CHEMOTHERAPY
A joint chapter in the history of chemistry and medicine ... ... *James Walker*
SOME MEDICAL CONTRIBUTORS TO CHEMISTRY ... ... *Trevor I. Williams*
TYPHUS AND CHEMOTHERAPY ... ... *A. W. Downie*
FACTOR ANALYSIS IN PSYCHOLOGICAL MEDICINE ... ... *Cyril Burt*

Annotations & News

Some medical conferences—French war-time researches—Anti-tuberculosis measures in Spain—Third interamerican congress of surgery—Three important new british journals—Bulletin of the World Health Organization—Surgical annals—Medical Bookman and Historian—Excerpta Medica—A new spanish abstracting and information service—A new microfilm service—An association of medical librarians—Publications and reports—Journals newly received—A medical publisher.

Historical Notes

PIERRE JANET ... ... *A. H.-S.*
WAYFARERS IN MEDICINE ... ... *Douglas Guthrie*
THE CHAMBERLENS AND THE MIDWIFERY FORCEPS ... ... *W. J. Bishop*
ST. THOMAS'S HOSPITAL 1106–1947 *L. T. Morton*
THE STORY OF QUININE ... ... *F. N. L. Poynter*
ANONYMUS LONDINENSIS ... ... *W. J. B.*

Book Reviews

Synopsis of allergy—Synopsis of anaesthesia—Curare—Cancer of the breast—Bioterapiya zlokachestvennikh opookholay—Differences in cancer death rates—Portiokarzinom—Herzinsuffizienz—Peripheral circulation—Atlas of dental histology—Textbook of leprosy—Atlas of histopathology of the skin—Dermadromes—Endocrine function of the hypophysis—Glands of destiny—Old age—Physical education—Magic and healing—Joseph Lister—The occasion fleeting—The doctor's job—The story of a doctor—The microscope—Physical background of perception—Anatomical pattern and sensory discrimination—Diseases of the basal ganglia and subthalamic nuclei—Sensory mechanisms of the retina—Hals-Nasen-Ohren- und Mundkrankheiten—Diseases of the liver—Pathological histology—Pathology of tumours—Child psychology—Shaping of psychiatry by war—Handbook of preventive medicine—Recent advances in public health—L.C.C. health and school medical report, 1946—Action of radiation on living cells—Radium dosage—Rheumatism and soft tissue injuries—Diagnosis in sterility—Surface and radiological anatomy—Ambulatory proctology—British surgical practice, Vol. I—Synopsis of orthopaedic surgery—The appendix—Chronic structural low backache—Poisons—Detoxication mechanisms—Dust—Tuberkulöse Reinfektion und Resistenz.

Shorter Notices

Ocular vertical deviations—Recent advances in medicine—Handbook of midwifery—Report on lunacy and mental deficiency, 1946—Diseases of the nervous system—Ulcer of the stomach, duodenum and jejunum—Traumatología ocular de urgencia—Symptoms and signs in clinical medicine—Sanitary inspector's handbook—A way of life for the child handicapped by cerebral palsy—The Peckham experiment—Man and animals: what they eat and why—Textbook of dietetics—Essentials for final examinations in medicine—Food poisoning—Propedéutica de patología circulatoria—Vital statistics and public health in the tropics—Child health and development—Tuberculosis and chest disease for nurses—Guide to anatomy—Gardiner's handbook of skin diseases—Current therapies of personality disorders—Pharmacology and therapeutics—Hey Groves' synopsis of surgery—Diseases of the nose, throat and ear—Experimental physiology—Insect pests—Practical physiological chemistry—Biology for medical students—Histology for medical students—Food inspection notes—Illustrations of regional anatomy—Midwife's text-book—Supplement to Lewis's library catalogue—Introduction to gastro-enterology—Praktikum der physiologischen Chemie—Nothing new under the sun—Spanish-English medical dictionary—Meat inspection—Panchito y el mosco anofeles—Essentials of materia medica—Gas and air analgesia—¡ Salud, madre campesina !—Good health with diabetes—Malaria en la cuenca del Lago de Maracaibo, 1942–1943—Old people—Synopsis of hygiene (Jameson & Parkinson)—Blood pressure and its disorders—The rhesus factor—Zählrohrmethoden im Forschungslaboratorium—Common skin diseases—The childbearing years—Cerebro-spinal fever—National Health Service Act, 1946—Malaria in Mauritius—Inter-allied conferences on war medicine—Massage and remedial exercises—Introduction to clinical perimetry—Cirugía—Modern treatment year book—Practical biology for students—Practical pharmacognosy—Handbook on diseases of children—Biologists in search of material: Peckham—Health services in England—Text-book of gynaecology.

Books Received

Films

Perfusion of the living animal [dog]
The humoral transmission of sympathetic impulses
The properties of acetylcholine
The physiology of the kidney
Catalogue of medical films

Guide to the Journals

THE MEDICAL RESEARCH COUNCIL

Its Origin, Constitution and Functions

F. H. K. GREEN M.D. F.R.C.P.

Assistant Secretary, Medical Research Council

The promotion of medical research on an organized scale has been accepted as a State responsibility in Great Britain for more than thirty-five years. The provision made by the State for this purpose is additional to the resources of universities and other independent foundations and institutions, but is itself substantial, amounting in terms of money expenditure in the current year to more than £770,000. These funds are administered by the Medical Research Council, a Government body though not, strictly speaking, a Government department. Like its sister organizations for industrial and agricultural research—the Department of Scientific and Industrial Research, and the Agricultural Research Council, respectively—the Medical Research Council is under the authority of a special Privy Council Committee of Ministers of the Crown. The Lord President of the Council—that is, of the Privy Council—is the Chairman of the Committee of the Privy Council for Medical Research and of the corresponding committees for scientific and industrial and agricultural research, and he is the Minister responsible to Parliament for the work of these three Government research bodies, an arrangement which assists effective co-operation between them.

Origin and Constitution

The Medical Research Council derives from the Medical Research Committee which was established in 1913 under the National Health Insurance Joint Commission to administer moneys provided for medical research under the National Health Insurance Act of 1911. This Committee had hardly had time to inaugurate its programme before it was confronted by the abnormal situation caused by the outbreak of the war of 1914-18. Co-operating closely with the Army Medical Service during that period, it promoted a large number of short-term studies relating to the treatment of wounds and injuries, to the etiology and treatment of tropical diseases, and to various other problems of military and civil hygiene, many of which have had permanent value. With the end of the war, and the passage of the Act of 1919 which established the Ministry of Health, there was a fundamental change in the administrative arrangements for the promotion of british government-aided medical research, one of the provisions of the new Act being to transfer this responsibility to a specially appointed Committee of the Privy Council. In 1920, accordingly, the former Medical Research Committee was reconstituted as the Medical Research Council under the statutory authority of the Committee of the Privy Council for Medical Research; it was granted a Royal Charter of Incorporation and the funds for its work were thereafter provided directly from the Treasury in the form of a grant-in-aid approved yearly by Parliament, an arrangement which has persisted ever since. The Committee of the Privy Council for Medical Research consists, in addition to the Lord President as Chairman, of the Ministers in charge of the principal State departments concerned with questions of public health in Britain and the Empire overseas; the Minister of Health is Vice-Chairman, and the Secretary of the Medical Research Council for the time being is *ex officio* Secretary; this means, in effect, that there is direct contact between the Council and its Minister, the Lord President.

The Council itself consists nowadays of twelve members, three lay and nine scientific, with a Secretary and other administrative officers. The present Secretary is Sir Edward Mellanby, G.B.E., K.C.B., F.R.S., whose own researches on rickets and other health problems are well known. Members of the Council retire in turn at regular intervals, but the aim is to ensure that its scientific membership always comprises a body of distinguished experts with first-hand experience of research in clinical medicine and surgery, and in the more important of the fundamental sciences on which these are based, as well as in some of the specialities of medicine. The scientific members of the Council are appointed by the Privy Council Committee, after consultation with the President of the Royal Society (as representing independent scientific opinion in the country), and with the Council itself. Of the three lay members of the Council, one must be a member of the House of Lords and one a member of the House of Commons. The Council appoints its own Secretary, and its administrative and scientific staff.

Functions

While research into the nature and causes of disease, and into improved methods for its prevention, diagnosis and treatment, naturally forms an extremely important part of the research programme of the Medical Research Council, that programme is of very much wider scope. It deals also with the fundamental sciences of medicine—physiology, biochemistry, genetics and the like; with problems of nutrition and of the maintenance of general human well-being, mental as well as physical; and with the normal and abnormal physiological and psychological reactions of the human being to his work and environment. It may deal, in fact, with almost any question involving the "human factor".

To advise it on the promotion of research in particular branches of medical science, the Council has the help of a large number of expert technical committees which it has itself appointed from time to time. The terms of reference of these different committees cover a very wide range of subjects; some of them are appointed on a short-term basis, to direct research on a single problem or group of problems, and are discharged on the completion of that task; others, such as the Accessory Food Factors Committee and the Chemotherapy Committee, are standing committees which assist the Council in the organization of long-term inquiries over an extensive field. Committees set up between 1939 and 1945 to direct research on urgent war problems included the Military and Royal Naval Personnel Research Committees and the War Wounds Committee; others were the Malaria Committee, the Jaundice Committee, the Penicillin

Clinical Trials Committee, the Committee on Tuberculosis in Wartime, and there were many more. Two examples of special interest at present are the Committee on the Medical and Biological Applications of Nuclear Physics (the medical by-products of modern atomic research), and the Colonial Medical Research Committee, the latter appointed jointly by the Council and the Colonial Office to direct work on nutritional and other questions affecting the health and well-being of colonial peoples, including, of course, the study of tropical diseases. In promoting research on problems of industrial welfare and efficiency the Council has the advice of its Industrial Health Research Board, and of special committees on Occupational Medicine, Occupational Physiology, Occupational Psychology, etc.

The Council itself meets about nine times a year, to survey and plan its programme, to discuss questions of policy, to consider requests from Government departments and other bodies for assistance in dealing with health and other "human" problems within their sphere, to receive the recommendations of its various expert committees, to review and, where necessary, increase the appointments to its staff, and to deal with applications from independent workers for financial aid in their researches. To assist in planning and directing investigations undertaken at the request of the Ministry of Health or other Government departments, the Council has usually appointed *ad hoc* committees, including representatives of the departments concerned. One such body which is very active at present is the Committee on Industrial Pulmonary Disease, originally appointed in response to requests from the Home Office and the Mines Department, and reconstituted in 1945 by arrangement with the newer Ministry of Fuel and Power; this Committee has sponsored a long-term programme of research, now being widely extended, on the problem of occupational lung disease in coalminers and other industrial workers.

In addition to having full executive control of its Parliamentary grant-in-aid, the Council is empowered by its Charter to accept and administer charitable benefactions by gift or bequest for the support of medical research. Its constitution also enables it to collaborate freely with other official or non-official organizations, either in Britain or abroad, which have functions similar to its own. Examples of such non-official organizations in Britain are the Lister Institute of Preventive Medicine, the Imperial Cancer Research Fund, the British Empire Cancer Campaign, the Wellcome Foundation and the Nuffield Foundation. An overseas body which has given generous help and co-operation to the Council in many different ways is the Rockefeller Foundation of New York.

National Institute for Medical Research and Associated Establishments

The Council's administrative headquarters is at 38 Old Queen Street, London, S.W.1, and its central research laboratories comprise the National Institute for Medical Research, at present situated at Hampstead, London, with associated Farm Laboratories and a special building for nutritional research, at Mill Hill, a few miles away. The institute at Hampstead—a former hospital, which was acquired by the Medical Research Committee in 1914—has become inadequate for growing needs, and it is hoped within the next two years to transfer its work to a new and much more commodious building on the Council's land at Mill Hill. The external structure of this new building was completed shortly before the war of 1939–45, and every effort is now being made to complete its internal equipment with minimum delay. Only laboratory research is done at the National Institute, the Council's programme of clinical investigations being carried out at other centres, as will be shown presently. Nevertheless, though much of the research work at the Institute is necessarily of a fundamental nature, a substantial part of it has an immediate bearing on clinical problems, and numerous field-studies in hospitals and elsewhere have been organized from the Institute; an instance is the new attack launched in 1946 on the etiology of the common cold; this is being carried out in a special unit at the Harvard Hospital, Salisbury, maintained jointly by the Council and the Ministry of Health. The research programme of the National Institute is a very wide one, divisible into the broad categories of physiology, pathology (including bacteriology, virus diseases and immunology), pharmacology, chemotherapy, biochemistry, endocrinology, and physics in relation to biological research. Diseases recently under intensive study there have included influenza, malaria and, during the war, the typhus fevers. A special responsibility of the Institute is the maintenance of standards of activity and purity for certain drugs, hormones, vitamin preparations and antitoxins, both in fulfilment of statutory obligations of the Council in the United Kingdom and, in many instances, on behalf of the World Health Organization (formerly the Health Organisation of the League of Nations). Sir Henry Dale, O.M., G.B.E., F.R.S., was the first Director of the National Institute; he was succeeded, on his retirement in 1942, by Dr. C. R. (now Sir Charles) Harington, F.R.S.

Clinical Research

Clearly, in any organized programme of medical research, prominence must be given to the study of problems of disease and injury as they are seen in patients—that is, to clinical investigations in hospital wards and outpatient departments. The Council has not established a special research hospital, deeming it preferable to take advantage of the available facilities and freer supply of clinical material at existing hospitals and the valuable opportunities to recruit and train new investigators which are provided by the day-to-day contact of research-workers with undergraduate and postgraduate students at academic centres. In conformity with this policy, the Council has for long maintained, wholly or in part, special units for clinical research at two London teaching-hospitals and at the National Hospital for Nervous Diseases, Queen Square, London. The oldest of these establishments is the Department for Clinical Research at University College Hospital, and it was here that the late Sir Thomas Lewis, F.R.S., carried out much of his famous work on diseases of the heart and blood-vessels. With the expansion of the Council's programme, the number of its special research groups dealing with clinical and other problems has been greatly increased in recent years; the Table appended shows the Council's chief existing research-establishments, other than the National Institute for Medical Research. The arrangement between the Council and the institution housing

PRINCIPAL RESEARCH ESTABLISHMENTS OF THE MEDICAL RESEARCH COUNCIL OTHER THAN THE NATIONAL INSTITUTE FOR MEDICAL RESEARCH AND ASSOCIATED ESTABLISHMENTS (SPRING 1948)

Subject	*Establishment*	*Place*	*Present Director of Unit or Department; or Head of Research Group*
General medicine	Department of Clinical Research	University College Hospital, London	E. E. Pochin, M.D., F.R.C.P. (*salary provided by Rockefeller Foundation*)
General medicine	Clinical Research Unit	Guy's Hospital, London	R. T. Grant, O.B.E., M.D., M.R.C.P., F.R.S.
Medicine (including nutritional and paediatric studies)	Department of Experimental Medicine	Cambridge University (*with temporary field-research unit at Wuppertal, Germany*)	Prof. R. A. McCance, Ph.D., M.D., F.R.C.P., F.R.S.
Diseases of the nervous system	Neurological Research Unit	National Hospital, Queen Square, London	E. A. Carmichael, C.B.E., M.B., F.R.C.P.
Problems of ear disease and deafness	Otological Research Unit	National Hospital, Queen Square, London	C. S. Hallpike, M.B., F.R.C.P., F.R.C.S.
Problems of vision	Vision Research Unit	Central London Ophthalmic Institute, Judd Street, W.C.1	H. Hartridge, M.D., F.R.S.
Treatment of cancer	Radiotherapeutic Research Unit	Hammersmith Hospital, London	Miss C. A. P. Wood, M.R.C.P., D.M.R.E. (*half-time*)
Industrial diseases and poisoning	Department for Research in Industrial Medicine	London Hospital	D. Hunter, M.D., F.R.C.P. (*part-time*)
Industrial health hazards, including injuries and skin diseases	Industrial Medicine Research Unit	Birmingham Accident Hospital and Rehabilitation Centre	J. R. Squire, M.B., M.R.C.P.
Burns	Burns Research Unit	Birmingham Accident Hospital and Rehabilitation Centre	,, ,,
Industrial pulmonary disease	Pneumokoniosis Research Unit	Llandough Hospital and other centres, Cardiff	C. M. Fletcher, M.D., F.R.C.P.
Actions of drugs in man	Clinical Chemotherapeutic Research Unit	Glasgow University and Killearn Hospital	J. Reid, M.D., M.R.C.P. (*part-time*)
Clinical aspects of endocrinology	Clinical Endocrinology Research Unit	Edinburgh University and Royal Infirmary	(*At present directed by a Committee*)
Nutrition	Human Nutrition Research Unit	National Hospital, Queen Square, London, and London School of Hygiene and Tropical Medicine (*with associated establishment in tropical Africa*)	Prof. B. S. Platt, C.M.G., M.B., Ph.D.
Nutrition (vitamin studies)	Group for Research on Nutrition	Lister Institute of Preventive Medicine, London	S. S. Zilva, D.Sc.
Nutrition (vitamin studies)	Dunn Nutritional Laboratory	Cambridge University	L. J. Harris, Sc.D.
Dental disease	Dental Research Unit	King's College Hospital, London	J. D. King, Ph.D., L.D.S.

a particular establishment varies from case to case, but the Council usually provides the medical and other scientific workers and the research expenses, the institution supplying accommodation and, in the case of the clinical units, the cost of feeding and nursing the patients. A statistical-research unit has been part of the Council's organization since the earliest days of its work; the unit is housed in the Department of Medical Statistics at the London School of Hygiene and Tropical Medicine, the Director of the unit, Professor A. Bradford Hill, himself giving part-time service to the Council.

Apart from its research establishments in Great Britain, the Council during the war despatched a number of field-research units overseas to carry out intensive investigations of health problems affecting the Fighting Forces. This principle is being extended in peacetime by the occasional appointment of special research groups to investigate health problems of importance to the Colonial Empire, at suitable centres abroad.

At the National Institute for Medical Research, at all the research centres listed in the Table, and at many others, the Council employs a whole-time scientific staff, appointed on either a permanent or a temporary basis. The large majority of the medical men or women directing, or working

Subject	*Establishment*	*Place*	*Present Director of Unit or Department; or Head of Research Group*
Bacterial chemistry	Bacterial Chemistry Research Unit	Lister Institute of Preventive Medicine, London	Sir Paul Fildes, O.B.E., M.B., F.R.S.
Bacterial chemistry	Group for Research in Chemical Microbiology	School of Biochemistry, Cambridge University	Miss M. Stephenson, Sc.D., F.R.S.
Cell metabolism	Cell Metabolism Research Unit	Sheffield University	Prof. H. A. Krebs, M.D., F.R.S. (*part-time*)
Problems of blood grouping	Blood Group Research Unit	Lister Institute of Preventive Medicine, London	R. R. Race, M.R.C.S.
Preparation of blood derivatives	Blood Products Research Unit	Lister Institute of Preventive Medicine, London	A. N. Drury, C.B.E., M.D., F.R.S. (*Hon. Director*)
Problems of transfusion	Blood Transfusion Research Unit	Postgraduate Medical School of London	P. L. Mollison, M.D., M.R.C.P.
Chemotherapy of malaria	Group for Research in Chemotherapy	Molteno Institute, Cambridge University	Miss A. Bishop, Sc.D.
Toxicology (with special reference to industry)	Toxicology Research Unit	Chemical Defence Experimental Station, Porton	J. M. Barnes, M.B.
Electromedical studies	Electromedical Research Unit	Ministry of Pensions Hospital, Stoke Mandeville, Bucks	R. B. Bourdillon, C.B.E., M.C., A.F.C., D.M.
Biophysics	Biophysics Research Unit	King's College, London	Prof. J. T. Randall, D.Sc., F.R.S. (*Hon. Director*)
Medical problems of nuclear physics (including research on health hazards)	Radiobiological Research Unit	Atomic Energy Research Establishment, Harwell	J. F. Loutit, D.M., M.R.C.P.
Molecular structure of biological systems	Unit for Research on the Molecular Structure of Biological Systems	Cavendish Laboratory, Cambridge University	M. F. Perutz, Ph.D.
Industrial physiology	Groups for Research in Industrial Physiology	London School of Hygiene and Tropical Medicine	(i) T. Bedford, D.Sc. (ii) H. C. Weston, F.I.E.S.
Occupational psychology	Applied Psychology Research Unit	Cambridge University	Prof. Sir Frederic Bartlett, C.B.E., M.A., F.R.S. (*Hon. Director*)
Occupational psychology	Group for Research in Industrial Psychology	Manchester and elsewhere	S. Wyatt, D.Sc.
Psychological and other "human" problems of the building industry (in relation to post-war reconstruction)	Group for Research on the Building Industry	Birkbeck College, London	Prof. C. A. Mace, M.A., D.Litt. (*Hon. Director*)
Medical statistics	Statistical Research Unit	London School of Hygiene and Tropical Medicine	Prof. A. B. Hill, D.Sc. (*part-time*)
Social medicine	Social Medicine Research Unit	Central Middlesex County Hospital	J. N. Morris, M.R.C.P., D.P.H., D.C.H.

in, these research establishments are whole-time servants of the Council who abstain from private practice. Among the subjects currently under study by members of the Council's staff at hospitals, university departments and other research centres outside the establishments listed in the Table are problems of disease in children, nutrition, clinical bacteriology, tuberculosis, chemotherapy, and the biological effects of radiation (with special reference to the treatment of cancer). Members of the Council's staff have pension-rights on retirement, which are provided through insurance policies to which both the Council and the member contribute.

Financial Aid to Independent Research Workers

While the greater part of the funds at the Council's disposal is devoted to the support of research by its own staff at the National Institute and elsewhere, an important fraction is, nevertheless, expended annually in the form of temporary grants made in aid of approved researches by entirely independent investigators at universities, hospitals and other institutions throughout the United Kingdom and, on occasion, overseas. These grants may be made variously for the personal support of the investigator on a whole-time or part-time basis, for the

provision of scientific or technical assistance to senior investigators, or for research expenses. Numerous investigations, at hospitals and elsewhere, by physicians or surgeons in practice are assisted by grants of one or more of these types. Where an application for a research grant comes within the field of interest of one of the Council's expert committees, the Council has the advice of the committee in considering it. An outstanding example of a research assisted by grants at a university centre during the war-years was the work by Sir Howard Florey and his colleagues at Oxford which led to the development of penicillin as a therapeutic agent. The grant system as a whole has produced a rich harvest of results of practical value.

Reference has been made above to the advantages, from the point of view of the recruitment and training of new research-workers in medical science, which are gained by the siting of most of the Council's clinical and other research establishments in academic centres. As a further aid to recruitment, the Council awards studentships for training in research methods to young graduates of special promise who are recommended for the purpose by the heads of the departments in which the training would be given. These studentships are tenable for a period of one year in the first instance, and are renewable up to a maximum of three years in all, subject to favourable reports from the supervisors of the work. One of the chief aims of the studentships is to make it possible for young men and women to contemplate, and display their fitness for, research careers who otherwise might be prevented by economic factors from doing so. Apart from these training studentships, which are tenable in the United Kingdom, the Council awards certain travelling fellowships to enable suitably qualified british workers to undertake periods of study and research at centres abroad. It has for long acted as the agent in Great Britain of the Rockefeller Foundation of New York, by awarding the travelling medical fellowships for british workers generously provided by that body, and it has its own series of travelling and research fellowships in tuberculosis, provided from the special benefaction in memory of Dorothy Temple Cross, of which it is the trustee.

Reports and Publications

Before the war the Council had to submit annually to Parliament a Report on its work, which was published. The latest of these Reports to be issued was that for 1938–39. The series was interrupted by war conditions, but the continuity of the narrative has been resumed with a six-year Report, reviewing the Council's many activities during the war-period, which has just been published (Spring, 1948)[1]. All the Council's publications are printed and sold by His Majesty's Stationery Office. Best known among them is the series of green-covered Special Reports, on a diversity of medical subjects, of which more than 260 have been issued. Others deserving special mention here are the seventeen War Memoranda, giving up-to-date advice on practical problems (such as the medical uses of sulphonamides), which were issued by the Council between 1939 and 1946, and the series of reports dealing with problems of industrial hygiene and efficiency which have been produced under the authority of the Council's Industrial Health Research Board. The Council's series of practical Memoranda is being continued in peacetime as a medium for the publication chiefly of summaries of existing knowledge, and the findings of *ad hoc* investigations. The results of the great majority of the researches supported by the Council are, however, reported directly by the investigators concerned, in papers contributed on their own initiative to medical and other scientific journals.

A *Bulletin of War Medicine*, consisting of abstracts and review-articles covering a large proportion of the contemporary medical and surgical literature from Allied and enemy countries, was produced by the Council from September 1940 till August 1946, with the help of the Bureau of Hygiene and Tropical Diseases.

Other Activities

In addition to its primary task of promoting and supporting medical research, the Council during the war-period undertook a number of special executive functions on behalf of the Ministry of Health, with which it always maintains close co-operation. Thus it was in large measure responsible for organizing the Emergency Blood Transfusion Service for air-raid casualties in the greater London area, and it established four depots near London for the collection and storage of blood for transfusion, the staffs of which managed effectively to combine with their routine duties the making of substantial new contributions to knowledge of their subject. The Council also established units for serum drying and blood grouping at Cambridge during the war, the former of which, under the direction of Dr. R. I. N. Greaves, did interesting pioneer work on new methods of drying and preserving proteins, and the latter, under the late Dr. G. L. Taylor, successfully followed up and extended the american discovery of the Rh factor and its practical significance in blood transfusion and in paediatrics; the Blood Group Research Unit is being continued under the direction of Dr. R. R. Race at the Lister Institute, London (see Table). Moreover—and this, too, has proved a development of more than ephemeral significance—the Council in 1939 set up and administered, on behalf of the Ministry of Health, an Emergency Public Health Laboratory Service to augment the existing public-health services of the country in combating epidemics of infectious disease such as were likely to arise from the abnormal conditions of war, and to keep a constant watch for any suspected instance of "bacterial sabotage". While the Service did not, in the event, have any example of "bacterial sabotage" to contend with, it proved so notably successful in elucidating and restricting outbreaks of infectious disease and bacterial food-poisoning during the war that it is being extended in peacetime as the framework of an organization for carrying out nation-wide investigations of problems of public health and epidemiology. At the request of the Government, the Council accordingly agreed to administer the peacetime Public Health Laboratory Service on behalf of the Ministry for an initial period of five years. Statutory authority for the Service has been provided in the National Health Service Act of 1946.

Earlier in this article it was mentioned that one of the functions of the Council at its periodical meetings is to "survey and plan its programme". It should be emphasized, however, that long-term planning, save in very broad outline (as by the appointment of a committee or establish-

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[1] *Medical research in war. Report of the Medical Research Council for the years 1939–45.* London: His Majesty's Stationery Office, 7s. 6d.

BRITISH BIOCHEMISTRY

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In Britain, biochemistry was an early and vigorous outgrowth from modern physiology as it developed under the leadership of men like Sir Michael Foster. Foster (1924) was a firm believer in the importance of the study of the history of his subject; and in the first of his Lane Lectures on "The History of Physiology", delivered in San Francisco in 1900, he expressed that belief in the following words:

> . . . What we know and what we think . . . is a stream which flows by us and through us, fed by the far off rivulets of long ago. As what we think and say today will mingle with and shape the thoughts of men in the years to come, so in the opinions we are proud to hold today, we may, by looking back, trace the influence of the thoughts of those who have gone before . . .

Our knowledge of history will reveal " . . . which of the thoughts of today are in the direct line of progress . . . " This alone is sufficient reason for our application to a profound and detailed study of the history of british biochemistry.

A number of books on specialized biochemical subjects provide us with specific examples of the power of the historical approach, but there has been nothing resembling a full account of the growth of the subject. Thus it is with hesitation that one attempts to sketch its history in a few pages. It is difficult to single out the contribution of one nation from the essentially international progress of science. However, even the most superficial consideration reveals that, in the biochemical field, Great Britain has contributed generously in terms of ideas, technical methods and hard work, the three essential components of creative scientific activity.

One Hundred Years Ago

In July 1947, the Chemical Society celebrated its centenary. A hundred years ago biochemistry in Britain was in its embryonic stage. At home, formative influences, such as the work of Thomas Graham, first President of the Chemical Society, were developing. Abroad, Liebig in Germany, and Pasteur and Claude Bernard in France, were leading the world in establishing the basic principles of the subject. Development in Britain was comparatively slow up to 1900, and british biochemistry must be said to be essentially a twentieth-century phenomenon.

The chemical activities of living creatures have excited the interest of the natural philosopher from the earliest days, and led him to many significant observations. In 1772 Joseph Priestley showed that green leaves produce oxygen, the first important observation in connexion with photosynthesis. In 1810 Wollaston discovered the sulphur-containing amino-acid cystine, so-called because he found it in urinary calculi. However important, these discoveries did not constitute part of a connected scientific discipline. The present vigorous growth of the subject had its serious, organized beginnings in the period towards the end of the nineteenth century when the rationalization of medicine was taking place. This movement brought human physiology to maturity as an independent science, after it had

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MEDICAL RESEARCH COUNCIL

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ment to carry out research over a considerable field), is rarely possible in medical science; the discovery of a preventive or cure for a particular disease is nearly always opportunist, depending upon the unpredictable occurrence of new clues for investigation, and upon the availability of research workers with the right type of knowledge and imagination to follow them up. Similar opportunist factors largely determine the range of the Council's research programme at any given time, and the number and staffing of its research establishments, though these are occasionally set up on an *ad hoc* basis to examine a particular health-hazard calling urgently for attention. Fleming's original work on penicillin was a good example of an opportunist investigation, arising in the course of studies of quite a different kind; on the other hand, the american discovery of streptomycin resulted from a "planned" attempt to find an antibiotic which would be therapeutically effective against the penicillin-resistant gram-negative microbes, though its still more remarkable action in certain forms of tuberculosis must have come as an agreeable surprise to its discoverers. Sometimes a long-term programme of "academic" research in physiology or biochemistry may itself lead suddenly to a discovery of immediate clinical value; while, as has been seen recently, the practical application of fundamental discoveries in the physical sciences may provide new and totally unexpected vistas of exciting exploration in biology and medicine. Thus, the finding that radioactive isotopes of the elements can be produced artificially and, while behaving chemically exactly like the stable elements, may be readily traceable in the living body by virtue of their radioactivity, has supplied a method of fascinating promise for investigating the detailed chemistry and physiology of vital processes, as also has the use of naturally-occurring, non-radioactive isotopes as "tracers" by means of mass-spectrography. With these new research weapons of unforeseeable range, with the record of practical achievement during the last decade, and with the recent advances in chemotherapy, in bacterial chemistry and the study of microbic antagonism to provide embarkation points for further voyages of discovery, the prospects for medical research are brighter now than at any previous time. It is to be hoped that the free co-operation and exchange of scientific information established between medical scientists of the Allied nations during the war may be extended on an international scale for the still more rapid advancement of knowledge aimed at increasing human health and well-being in the years to come. It will be a task of the Medical Research Council to assist such co-operation to the fullest extent possible and to ensure that, so far as Great Britain and the Colonial Empire are concerned, the opportunities of the coming years are used to good effect.

functioned for a long period as a minor appendage of Anatomy. Biochemistry began then as a lesser aspect of physiology, but developed rapidly to play its present leading role.

The preponderant influence of medicine has remained a feature of biochemistry in this country. Although agriculture provides a vastly richer source of fascinating problems, it has had a much smaller influence. It may be significant that the decline of british agriculture had already set in before biochemistry had begun its vigorous development.

The advance of biochemistry depended primarily upon the enormous edifice of organic chemistry built mainly by the Germans during the last century. It is a disadvantage, perhaps still felt, that we in this country were late in recognizing this fact. As late as 1913, the late Sir Frederick Gowland Hopkins, in his presidential address to the Physiological Section of the British Association, found it necessary to reiterate the appeal made by Justus Liebig to the Chemical Section of the same organization in 1837, pleading for the closer integration of organic chemistry and biology. Today we are able to look back on many achievements based on that lesson. However, this alone would not have given us modern biochemistry, which, rightly, is concerned not mainly with the analysis and synthesis of substances of biological importance, but with the manner in which living organisms achieve chemical changes.

This brings us into the field of colloid chemistry and catalysis. About the middle of the last century, Thomas Graham characterized the colloidal state, and his colleague, Sidney Ringer, investigated the balanced activities of inorganic constituents in regulating energy discharges in living cells. Ringer made his observations long before Arrhenius put forward his Ionic Theory. It is an interesting sidelight on the narrow outlook of many scientists of the time that Arrhenius was unaware of how Ringer's observations bore eloquent testimony to the correctness of the ionic concept.

Physical chemistry provided one of the most delicate and successful tools used in biochemistry. Thudichum, Archibald Garrod, MacMunn and F. G. Hopkins, of the developing school of british biochemists, all used it to make observations of the first importance, before the end of the nineteenth century. Among the many brilliant observations of the ill-fated MacMunn (1886) was the discovery in 1886 of "myohaematin" or "histohaematin"—the substance now better known as cytochrome. This observation did not attract the attention it deserved because of the attacks of the famous continental biochemist Hoppe-Seyler, who did not accept it. MacMunn was so discouraged that he gave up his researches. Hopkins used the spectroscope in his classical work on the pterine pigments in butterfly wings.

Archibald Garrod was one of the first to achieve that revolution in thought by which metabolism came to be considered in terms of enzyme-catalyzed paths rather than as a gross process of combustion. He was the father of biochemical genetics, and it is only now that his views are producing a rich harvest in the work of the american school led by G. W. Beadle and E. L. Tatum. It is to the credit of a number of british workers that they carried this line of development forward during the long interim period. Prominent among them were V. A. Onslow, Mrs. Onslow, J. B. S. Haldane and R. Scott-Moncrieff, all of whom worked in Hopkins' laboratory.

It is not possible to pass to the twentieth century without mentioning Thudichum, a prominent contemporary of Garrod's. Thudichum gave us the first firm chemical data on a number of the constituents of nervous tissues: he founded the chemistry of the brain.

Hopkins, Harden and their Collaborators

Gowland Hopkins dominated the development of biochemistry for the next forty years. By 1900 he had contributed his elegant work on the pterine pigments. In 1898 he and Pinkus had developed a greatly improved method for the crystallization of egg-albumin. In 1901 he and S. W. Cole isolated the amino-acid tryptophan from a tryptic digest of casein. Thus within two years he participated in two major contributions to protein chemistry. Then followed his nutritional studies, which established the nutritional importance of tryptophan and led to his discovery of the accessory food substances—the vitamins.

Hopkins inspired many lines of work now actively pursued all over the world. In some of them he conducted the classical experiments himself. The modern concept of the metabolic process directly concerned with energy production by working muscle, dates back to the work of Walter Fletcher & Hopkins in 1907. They confirmed previous observations that, when a muscle is made to contract in the absence of oxygen, lactic acid is produced. They also showed that the lactic acid is removed and glycogen reappears when the muscle is allowed to resume oxidative metabolism. This provided the essential idea of the muscle-cycle and of other glycolytic systems.

At about the same time Harden and his collaborators at the Lister Institute in London were working on the chemistry of the fermentation processes. This work was to merge eventually with the developments of Hopkins and Fletcher and in particular with the contributions of the German-led school in Europe, in the great burst of advances in our knowledge of the processes of glycolysis, which took place after the first World War.

In 1897 Buchner, in Germany, had shown that an extract of crushed yeast, from which all intact cells had been removed, retained the capacity to ferment sugars. Harden and Young studied this cell-free fermentation process and showed that the extract converted certain sugars to fructose diphosphate. This discovery ranks with the greatest in the history of the subject. Besides showing the importance of the phosphate esters in metabolism, Harden & Young (1904) were the first to demonstrate the existence of a co-enzyme: a heat-stable, dialyzable substance needed to activate an enzymic system. In 1904 they showed that such a substance, which they called co-zymase, now known as co-enzyme I, was essential in the yeast fermentation process.

Later, Robison, a pupil of Harden, discovered hexose monophosphate. Also, through a chance observation, he was able to show that the phosphate esters are concerned in the formation of calcium phosphate in calcifying tissues. In 1927, Eggleton and Eggleton, working at University College, London, showed that a new form of organic phosphate was involved in glycolysis. This was named phosphagen. It proved to be the substance, phospho-creatine, which had been isolated from muscle by the Americans Fiske and Subbarow in the same year.

These advances, combined with new knowledge of cellular oxidation-processes, marked the opening stages of the tremendous development in the study of cellular metabolism which took place between the two wars. In Britain, a large part of the work was concentrated in Hopkins' laboratory. Later it grew up in other centres mainly under the guidance of his former pupils, R. A. Peters at Oxford and H. A. Krebs in Sheffield.

The realization of the importance of carriers in biological oxidation processes began in 1921 with Hopkins' isolation of glutathione. This was followed in 1925 by Keilin's confirmation of MacMunn's discovery of cytochrome and his demonstration of its components and their role in cellular oxidation. M. Dixon, D. E. Green, Keilin again and many other workers in the Cambridge school contributed a mass of information on the nature of oxidation paths in the cell.

Bacterial Chemistry

In the same school J. and D. M. Needham were studying the glycolytic systems in mammalian striped muscle and other tissues. J. H. Quastel and Marjory Stephenson were laying the foundations of the study of bacterial metabolism, using washed suspensions of bacteria. Since that time Quastel's interests have extended to a diversity of fields. The traditional study has been carried on by Stephenson and her school with a regular series of important discoveries. Stephenson's studies have been confined to dynamic aspects of the subject. The other famous group of bacterial chemists in this country, built up by Sir Paul Fildes and B. C. J. G. Knight at the Middlesex Hospital in London, devoted its attention to the nutritional requirement of bacteria and added a great deal to our understanding of vitamins and the nature of parasitism. The high-light of the work of this school was Woods' (1940) observations on the nature of the antibacterial action of the sulphonamides.

R. A. Peters, who has held the chair of biochemistry at Oxford for many years, has contributed much to the science, both as a philosopher and as a practical man. He was one of the first to link a vitamin with a metabolic process (Peters & Thompson, 1934) by showing that vitamin B_1 has a co-enzymic effect in the oxidation of pyruvate in brain. A recent outstanding achievement of his school was the production of BAL (British Anti-Lewisite).[1]

H. A. Krebs is the author of a great deal of important work on cell-metabolism. He is probably best known for his work on mammalian urea-production via the so-called ornithine cycle, or Krebs urea cycle (Krebs & Henseleit, 1932), and for his work (Krebs & Johnson, 1937) demonstrating the function of tricarboxylic acids in cell-metabolism.

Like Krebs, J. H. Quastel has produced a large volume of work on cell-metabolism. One of his most fruitful contributions was his demonstration (Quastel & Wooldridge, 1928) that malonate inhibited the oxidation of succinate by the enzyme succinic dehydrogenase. The degree of inhibition depended on the relative concentrations of the substrate (succinate) and the inhibitor (malonate). This phenomenon was called competitive inhibition. The principle was invoked by Woods to explain the competition between *p*-aminobenzoic acid and sulphanilamide in their effect upon the growth of bacteria. Sulphanilamide prevents growth, but if *p*-aminobenzoic acid is present the amount of growth increases roughly in proportion to its concentration. Competitive inhibition has become one of the principal concepts of modern chemotherapeutic theory.

Biological Organic Chemistry

The advances which have been described show the very great importance of organic chemistry in the development of biochemistry. However, there is a great tradition of biological organic chemistry in this country which has developed on rather different lines from those already described. The difference between the two traditions is one of emphasis, and each has contributed to the growth of the other.

One of the achievements of organic chemistry arising out of the work of Hopkins was C. R. Harington's synthesis of glutathione (Harington & Mead, 1935). Harington is an outstanding representative of the school of biochemistry built by George Barger. Barger studied chemical aspects of pharmacology, chemotherapy, hormones and vitamins. Harington and he were responsible for the classical work on the hormone thyroxine. In 1926 Harington (1926a) was successful in isolating it from thyroid glands. Shortly afterwards he established its chemical structure (1926b). The work was brought to a triumphant conclusion by the synthesis of thyroxine (Harington & Barger, 1927).

During the course of this century Barger achieved many syntheses and characterized numerous biologically-important substances. His greatest interest was in the so-called simpler natural bases. In 1905 he and Jowett came near to the synthesis of adrenaline. This synthesis was achieved by H. D. Dakin and simultaneously by continental workers. Barger collaborated with Sir Henry Dale in much work on the sympathomimetic amines. They isolated histamine from the animal gut and synthesized tyramine. Barger also synthesized methionine and carnosine and was associated with A. R. Todd and others in their work on the synthesis of vitamin B_1. Barger was trained as a botanist as well as an organic chemist and in the course of his life made contributions to the chemistry of the alkaloids and glycosides.

Dale's most striking biochemical work was done in collaboration with H. W. Dudley (1927). These two workers were the first to isolate acetylcholine. Dudley was a brilliant worker who will be remembered for contributions such as the discovery of the enzyme glyoxalase (Dakin & Dudley, 1913), which converts methyl glyoxal to lactic acid.

In the last twenty years cyclopentenophenanthrene derivatives have been shown to have a variety of important biological functions as sex hormones, heart drugs, carcinogenic agents, bile acids, etc. British workers have played an essential part in this development. In 1932 Rosenheim & King put forward the idea that the sterols and bile acids were cyclopentenophenanthrene derivatives. This had a revolutionary effect and led to the rapid solution of the structure of many representatives of the above types of compounds. Prominent among the workers in this field were the british chemists Cohen, Cook, Dodds, Hewett and Kon.

[1] [See also *BMB* 1198.—ED.]

A little earlier Marrian (1930), working at University College, London, had isolated the important female sex hormone, oestriol, from pregnancy urine. This was his first outstanding success among his important studies of the chemistry of the sex hormones.

For many years J. W. Cook, Kennaway and their collaborators searched among the coal-tar products for those responsible for its carcinogenic effects. They isolated and identified many polycyclic hydrocarbons with carcinogenic properties. Others they synthesized. Cook and E. C. Dodds initiated the study of synthetic oestrogenic substances. They were able to show that the oestrogenic effect could be obtained with a wide variety of chemical substances. The same group of workers established the important connexion between the oestrogenic and carcinogenic effects.

The University of St. Andrews is famed for its school of sugar chemistry which grew up at the end of the last century under the leadership of Purdie and Irvine. Purdie developed a gentle method for the methylation of the hydroxyl groups of sugars, whereby it became possible to carry the study of sugar chemistry forward after it had reached an impasse. Purdie's method opened the way for the study of the ring-structure of the monosaccharides and the way in which they are joined together to form higher sugars. The leader of british sugar-chemistry today is Sir Norman Haworth. He was formerly at St. Andrews and now heads the chemistry school at Birmingham. In 1925 he demonstrated the pyranose ring structure in sugars. A number of his collaborators, led by E. L. Hirst (Ault *et al.* 1933), achieved the first successful synthesis of vitamin C.

Britain has contributed relatively little chemical work in the field of vitamins. Besides the synthesis of vitamin C, contributions have been made to the chemistry of vitamin D and vitamin B_1. Rosenheim & Webster produced vitamin-D activitity by irradiating phytosterols in 1925; in 1932 a team of workers, Askew *et al.*, were successful in isolating pure crystalline vitamin D_2 from irradiated ergosterol. The contributions of Todd, Bergel and their group to the synthesis of vitamin B_1 have already been mentioned.

Todd was a pupil of Sir Robert Robinson, the leading british organic chemist. Robinson is best known for his work on two widespread groups of organic compounds occurring in the plant kingdom, the alkaloids and the anthocyanins and flavones. He achieved his classical tropinone synthesis in 1917; in 1924 Pratt & Robinson synthesized the anthocyanidin pelargonidin; ten years later Robinson (1934) announced his method for the synthesis of the complete anthocyanin molecule.

Plant-Biochemistry

Although many able organic chemists in Britain have devoted themselves to the study of plant products, the british tradition in plant-biochemistry is not strong. The work of Raistrick and his colleagues on the constitution of many substances which are produced by the metabolic action of moulds upon simple sugars is a major contribution to our understanding of plant metabolism. Schryver's small school at South Kensington did much work in the field of analysis and isolation of plant products. Schryver was succeeded by A. C. Chibnall, who has an international reputation for work in this field, in particular for his classical work on the chemical constitution of the plant- and insect-waxes and his contributions to our knowledge of the amino-acid composition of proteins.

Two important recent advances in plant-biochemistry have been due to british workers. In 1940 C. S. Hanes reported the biosynthesis of one component of starch, and in the same year R. Hill demonstrated the production of oxygen by isolated chloroplasts.

Recent Developments

R. Hill (1939) has had a long association with biochemistry in Britain. His early work on haemoglobin formed part of the impressive series of studies on the respiratory function of the blood which started in Cambridge before the first World War. Many famous names are associated with that work: Barcroft, Haldane, Keilin, Roughton and others.

It has not been possible to consider all the important biochemical developments which have taken place in Great Britain. No mention has been made of the influence of men like Sir William Bate Hardy, Benjamin Moore and Raphael Meldola. Hardy contributed most to the field of biophysics, which has not been given its due attention in this survey. Physico-chemical methods have been greatly developed by british workers during the last two decades. Very recently Martin & Synge (1941) developed the partition-chromatogram and immediately effected a revolution in the amino-acid analysis of proteins. They were able to make great advances towards the solution of the problem of the quantitative separation of the mono-amino-acids, which had baffled the organic chemist for decades. Astbury, Bernal, Crowfoot and others developed *x*-ray analysis and applied it to the elucidation of the structure of biological molecules such as the fibrous and crystalline proteins. Bernal settled the doubt as to the detailed structure of cholesterol by this means. Confirmation of his view came from the field of surface chemistry, which had been developed in this country by E. K. Rideal and N. K. Adam.

Recent achievements such as the production of british anti-lewisite and penicillin represent the highest fruit of the british tradition. Each of them is a more than full justification for the many lines of earlier work upon which they depended: microbiology, enzyme studies, organic chemistry and many others. With a very limited scientific personnel, Britain is now faced with the difficult task of deciding which of the many profitable fields of biochemical study open to us will be the most profitable. It is not the task of the writer to propose a solution here. It is sufficient to say that whatever the general lines of the future development in british biochemistry, we can confidently expect it to continue to produce some of the world's best and most original contributions.

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CHEMOTHERAPY: A JOINT CHAPTER IN THE HISTORY OF CHEMISTRY AND MEDICINE

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> *Chemistry is an Art, whereby sensible bodies contain'd in vessels, (or at least capable of being contained therein and render'd sensible;) are so chang'd, by means of certain instruments, and especially fire, that their several powers, and virtues are thereby discover'd; with a view to the uses of medicine, natural philosophy, and other arts and occasions of life.*
>
> H. Boerhaave
>
> *A new method of chemistry*, translated by P. Shaw & E. Chambers, London, 1727, p. 51

The relationship between chemistry and medicine, so intimate at the present time, extends backwards through the centuries to the distant times when primitive man, in his efforts to mitigate the hardships of life, came to associate in his mind, in his folk-lore, and in his writings, the ingestion of certain crude vegetable drugs—mineral drugs came later—with the alleviation of some of his bodily ailments. The Ebers papyrus, which dates from about the 14th century B.C., is actually a text-book of materia medica and is believed to contain a reference to colchicine (Sharp, 1909), whose biological effects are still the subject of intensive study. The name of Galen (131–201 A.D.) is familiar to students of the history both of medicine and of chemistry, and is preserved to us to this day in the term "galenical". Such was Galen's influence that his teachings held sway for over a thousand years, until the iconoclastic figure of Paracelsus (1493–1541) came upon the scene, introducing the "iatrochemical" period, to be followed closely by Vesalius (1514–1564), the father of anatomy, and by Harvey (1578–1657), the father of physiology. To these three men we owe the foundations of modern medicine, which has advanced with ever-increasing vigour since their time, particularly during the past 100 years with the growth of our precise and intimate knowledge of chemistry and pharmacology, and the rise of microbiology. As a sign of the times, the oldest national chemical society in the world was founded in London in 1841 under the chairmanship of Thomas Graham, the father of colloid science, and recently celebrated the centenary of its foundation, the observance of the occasion having been postponed because of the war. In 1858 Kekulé and Couper crowned the work of Dalton and Frankland with the structural theory of organic chemistry and paved the way for synthetic organic chemistry in the modern sense. Pharmacology, too, was put upon a sure foundation about the same time by Buchheim who emphasized that "die Arzneimittellehre ist eine theoretische, d.h. erklärende Wissenschaft und hat die Aufgabe, uns die auf die Arzneimittel bezüglichen Kenntnisse darzubieten, durch welche die Richtigkeit unseres Urteils über ihre Brauchbarkeit am Krankenbett gefördert werden kann" (Schmiedeberg, 1912). Following upon these events are recorded the foundation of bacteriology by Pasteur and Koch, its systematization by Cohn, Lord Lister's zealous advocacy of antisepsis, and the study of toxins and antitoxins (Roux; von Behring), which was placed on a precise quantitative basis by Ehrlich. The great advances in microscopy in the early part of the century made by Lord Lister's father, Joseph Jackson Lister, and later by Abbe, coupled with selective staining (Weigert; Ehrlich) and other improvements in microbiological methods, led to the discovery, towards the end of the century, of protozoal parasites as the causes of disease, the names of Manson, Laveran and Bruce coming readily to mind in that connexion. The position at the turn of the century was therefore that chemistry, pharmacology, microbiology and parasitology had severally made distinguished progress during the nineteenth century but no one science had markedly made its influence felt upon any of the others. It was therefore

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Continued from page 360

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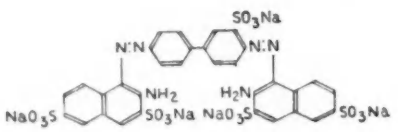
a timely development when Ehrlich brought about a fusion and founded experimental chemotherapy, which embraced them all. Although he took a medical qualification Ehrlich did not take his ideas from medicine, supporting them with chemical knowledge, but conversely, to quote his own words (1909), "ich während meiner ganzen wissenschaftlichen Arbeit mich bemüht habe, das, was uns die Chemie gelehrt hat, auch der Medizin nutzbar zu machen". In searching for substances which should be lethal to infecting parasites and yet harmless to the infected host, Ehrlich sought to apply what a life-time's study of the selective affinities of chemicals for cells had taught him.

Chemotherapy of Protozoal and Spirochaetal Infections

Early Trypanocidal Dyes : Bayer 205

The successful development of chemotherapy as an experimental science depended upon the transmission of diseases to experimental animals and Laveran & Mesnil's demonstration (1902a) that trypanosome infections could thus be studied in mice provided Ehrlich with a convenient subject for study. With Shiga, Ehrlich (1904) showed that the dye trypan-red (I) had the effect which he sought but a more successful substance was found by Mesnil & Nicolle (1906) to be trypan-blue (II), which found practical application in piroplasmosis of domestic animals (Nuttall & Hadwen, 1909). A further substance studied by Mesnil and Nicolle was trypan- (or afridol-) violet (III) which, although not applied practically, is of great historic interest as being the first representative of the symmetrical urea type of drug, further developed in 1912 by Heymann (see Roehl, 1926a), who replaced the chromophoric azo-linkage by amide groups, thereby abolishing undesirable tinctorial properties and ultimately yielding Bayer 205 (germanin, suramin, Fourneau 309) (IV), one of the most remarkable, and probably the most complex, of drugs ever synthesized. The lineal descent of Bayer 205 from trypan-blue is reflected biologically in the fact that trypanosomes which have acquired resistance to trypan-blue are also resistant to Bayer 205 (Leupold, 1924), acquired resistance to one compound being usually accompanied by resistance to chemically-allied substances only. Bayer 205, or suramin, to give it its non-proprietary pharmacopoeial name, is one of our most valuable drugs in the chemotherapy of sleeping sickness, being useful prophylactically and also for the treatment of established infections provided the central nervous system is not involved.



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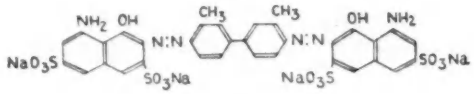

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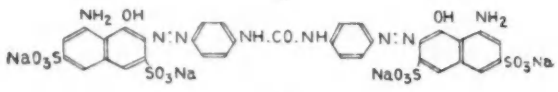

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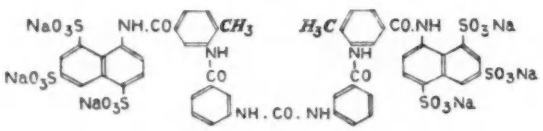


IV

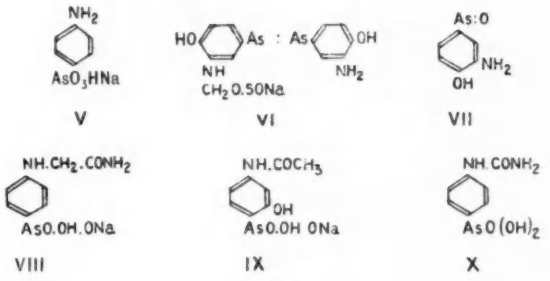
Arsenicals

Although inorganic arsenic had been used empirically for trypanosomiasis in domestic animals for some time (Braid, 1858; Livingstone, 1858) the results can be described, at best, as indifferent (Laveran & Mesnil, 1902b) and a marked advance was Thomas's demonstration (1905) in Liverpool that atoxyl was an effective agent in trypanosomiasis. Stimulated by this observation, Ehrlich & Bertheim (1907) proceeded to the elucidation of the correct constitution of atoxyl (V) and then to the development of salvarsan, which Ehrlich & Hata (1910) introduced for the treatment of syphilis, the causative agent having just previously been demonstrated by the zoologist Schaudinn. Shortly afterwards, neosalvarsan, or neoarsphenamine (VI), was introduced and, with one or two analogous derivatives of the same parent compound, constituted chemotherapy's greatest accomplishment for many years.

It was found that while atoxyl was active in vivo it was not active in vitro against trypanosomes and it was concluded that reduction in the body to the trivalent arsenoxide stage preceded trypanocidal action and, similarly, as there is a latent period of several hours before spirochaetes, or trypanosomes, are cleared from the blood of animals treated with the arsphenamines, it was again concluded that conversion to the arsenoxide precedes chemotherapeutic action (Voegtlin & Smith, 1920). Although the arsenoxide is considered to be the form in which the arsphenamines exert their spirochaeticidal action in the body, Ehrlich and Hata had rejected this substance (VII) as being too toxic for clinical use, but work in the last decade has clearly shown that it has as satisfactory a chemotherapeutic index as the arsphenamines. There is good evidence to show that the arsenoxide interferes with the turnover of sulphydryl groups in the parasite and by this interference a vital metabolic reaction is stopped. Conversely, by competition with the thiol groups of the parasite, the addition of glutathione and certain other thiol compounds both in vitro and in vivo protected trypanosomes against the arsenoxide by combining reversibly with the latter. An elegant application of this affinity of thiol groups for arsenic is to be found in BAL (British Anti-Lewisite), 2:3-dimercaptopropanol[1], in which it was argued that, by forming a ring with two adjacent thiol groups, a less readily reversed detoxication of the arsenic could be achieved (Stocken & Thompson, 1946). So far, therefore, out of the hundreds that have been studied, those arsenicals which have attained a place in clinical medicine are: the arsphenamines and mapharside (VII), which are used in syphilis; tryparsamide (VIII) and orsanine (IX),

[1] [See *BMB* 1198 in this number.—Ed.]

which are used in trypanosomiasis on account of the ease with which these drugs can penetrate into the central nervous system and so reach parasites inaccessible to Bayer 205; and carbarsone (X), which has received some application in amoebic dysentery along with the alkaloid emetine and the iodohydroxyquinolines.

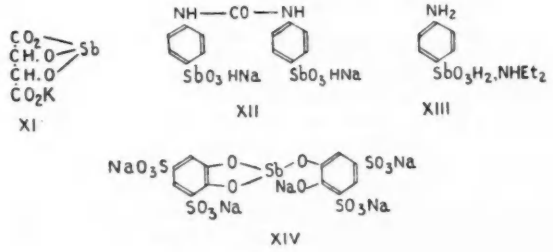


V VI VII

VIII IX X

Antimonials

The use of antimony, the congener of arsenic in the Periodic System of the elements, has not developed to the same extent as that of the latter, due, in some measure, to intrinsic chemical disadvantages. Although Plimmer & Thomson (1908) found at the Lister Institute that rats infected with trypanosomes could be freed from parasites by tartar emetic (XI) and its sodium analogue, the most significant application of antimony in chemotherapy has been in kala-azar. In 1912, Vianna found that cutaneous leishmaniasis could be influenced by tartar emetic, and the introduction by Rogers (1915) of tartar emetic in India for the treatment of kala-azar replaced symptomatic treatment, which was practically invariably unsuccessful, by specific therapy. Since 1915, a number of pentavalent antimony compounds have received careful clinical trial in kala-azar, and Brahmachari's urea-stibamine, of which the main component is the symmetrical urea (XII) (Gray, Trevan, Bainbridge & Attwood, 1931), and neostibosan (XIII) have come into fairly wide use for the treatment of infections in India and China. On the other hand, mediterranean infections respond better to tartar emetic and fouadin (XIV). Many compounds of antimony with hydroxy acids have been tested for chemotherapeutic activity but, of these, only two, sodium antimony tartrate and its potassium analogue (tartar emetic), are used in medicine at the present time. Similarly, trivalent antimony compounds with phenols and mercaptans are well known. Of the former, fouadin (stibophen) came into extensive use in 1929 (Khalil *et al.*) and partly displaced tartar emetic in the treatment of schistosomiasis, the latter having come into prominence for this purpose in 1918 (Christopherson). Still later, in 1936, anthiomaline was introduced by french workers but current opinion is divided as to the value of this drug.

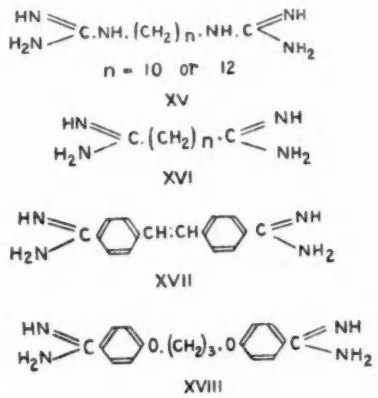


XI XII XIII

XIV

Diamidines

In considering the mode of action of Bayer 205, von Jancso & von Jancso (1934) considered that the drug interfered with the sugar metabolism of trypanosomes. It was known that hypoglycaemia occurs in experimental trypanosome infections, and that trypanosomes, furthermore, consume large amounts of glucose. The von Jancsos (1935; also Schern & Artagaveytia-Allende, 1936) therefore proceeded to an examination for trypanocidal activity in vivo of the synthalins—discarded several years previously after a brief but inglorious career as an oral substitute for insulin—and did indeed observe activity, but not because of any effect on sugar metabolism, since Lourie & Yorke (1937) showed synthalin to act directly on trypanosomes in vitro in high dilution. With the chemical collaboration of King (King, Lourie & Yorke, 1937), it was found that the guanidine groups of synthalin (XV) could be replaced by other groups, and, in particular, by amidine groups giving diamidines (XVI), which were yet more active and less toxic than the diguanidines. Later, it was found that the alkylene chain could be replaced by aromatic groups (King, Lourie & Yorke, 1938) and further development of this type in the May and Baker laboratories has led to stilbamidine (XVII), propamidine (XVIII) and pentamidine (Ashley *et al.* 1942). Like Bayer 205, these compounds are markedly active in the early stages of *T. gambiense* and *T. rhodesiense* sleeping sickness but their most fruitful application has been in kala-azar, in which antimony-resistant cases have responded, and in babesiasis in domestic animals (Yorke, 1944). Propamidine has also received some application as a topical antibacterial agent but marked toxicity is a disadvantage shared by these compounds.



n = 10 or 12

XV

XVI

XVII

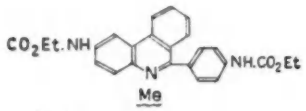
XVIII

Phenanthridinium Compounds

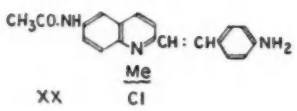
In 1931, Morgan & Walls at Teddington began a comprehensive investigation of phenanthridine compounds based on the readily available 2-aminodiphenyl. Biological tests from time to time failed to reveal promising

activity until Browning and his collaborators encountered trypanocidal activity in quaternary salts from 3 (and 7) -amino-9-*p*-aminophenylphenanthridine derivatives (Morgan *et al.* 1938). Further investigation of this series has revealed substances with pronounced activity against the relatively resistant *T. congolense* infections (Walls, Browning, Calver & Leckie, 1945), and recently activity against *T. cruzi* has been detected (Walls *et al.* 1946), only one other drug (Bayer 7602 Ac) being notably active against the latter parasite, which is refractory to other classes of trypanocidal drugs.

It is of interest to note that the phenanthridinium compounds bear a distinct resemblance chemically to trypanocidal styrylquinolines, which were previously studied by Browning and Cohen with their collaborators (Browning, Cohen, Ellingworth & Gulbransen, 1926, 1929), as shown by the following formulae (XIX, XX) of highly active compounds in the respective series, the elimination of the -CH : CH- group being one which the chemist can envisage with equanimity:—



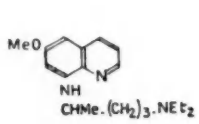
XIX



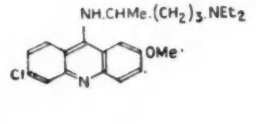
XX

Antimalarials

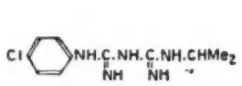
The time-honoured use of quinine in the treatment of malaria is a genuine example of chemotherapeutic action and, beyond Ehrlich & Guttmann's (1891) empirical trial of methylene blue, no further progress in the chemotherapy of malaria took place until a precise testing method (Roehl, 1926b) rendered the laboratory examination of drugs feasible. Plasmochin (pamaquin, XXI) was first elaborated (Roehl, 1926b), based, it is said, on Ehrlich's early methylene-blue experiment, and followed, a few years later, by atebrin (mepacrine XXII) (Kikuth, 1932), which is said to have been based not on methylene blue but on acriflavine, the Germans being impressed with Browning's exploitation of acriflavine during the first World War. Quinine and atebrin dominated the therapy of malaria until the entry of Japan into the late war rendered the former unobtainable, and an added stimulus was thereby given to the search for still further antimalarial drugs. Shaking themselves free from the tradition that antimalarial activity should be sought among derivatives of quinoline and acridine, Curd, Davey & Rose (1945) of Imperial Chemical (Pharmaceuticals), Ltd. accomplished a remarkably successful search with the ultimate production of paludrine (XXIII), which is the most versatile antimalarial drug yet discovered. Recent american work has revealed promising activity in resochin (XXIV), which may be regarded as being derived from mepacrine (XXII) by ablation of the methoxylated benzene ring, and a homologue, sontochin; these two drugs were encountered initially in the I.G. laboratories but were not brought into full production by the Germans because of economic wartime difficulties.



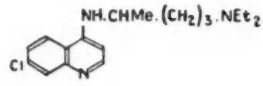
XXI



XXII



XXIII

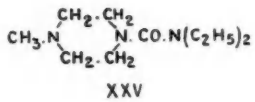


XXIV

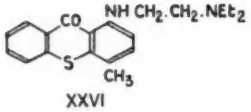
Chemotherapy of Helminthiasis

Numerous locally acting drugs are known which will expel parasitic worms from the gastro-intestinal tract but it is doubtful if any of these compounds conform to the usual criteria of chemotherapeutic agents, and the lack of suitable experimental animals in which the infections can be maintained and studied has hampered research on the chemotherapy of helminthiasis. Within the past year, however, notable advances in the chemotherapy of filariasis have emerged from the use of a natural filarial infection of cotton rats for the routine examination of drugs. A number of compounds of the cyanine-dye type were first shown to be active in the cotton rat (Welch *et al.* 1947; Brooker & Sweet, 1947), and still more recently, marked activity has been discovered among piperazine derivatives, out of which hetrazan (XXV) has been selected for further study (Hewitt *et al.* 1947).

Miracil (XXVI), which was found to be active in experimental schistosomiasis, has proved disappointing in human clinical trials.



XXV



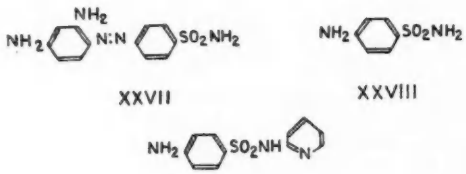
XXVI

Chemotherapy of Bacterial and Virus Infections

Antibacterial Chemotherapy

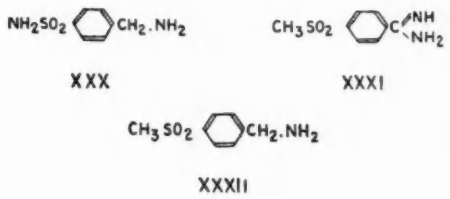
In discussing antibacterial agents it is customary to think in terms of disinfectants, antiseptics and chemotherapeutic agents but, strictly speaking, the one type merges with the other in the order given and differences are relative ones depending upon toxicity to the host. Disinfectants are usually gross and indiscriminate poisons for cells and need not be further considered here. Antiseptics are usually applied topically and, as they are frequently of such low

toxicity to the cells of the host that they may be used with safety on sensitive tissues, they can often be classed with the chemotherapeutic agents. Bacteria, in contrast with protozoa, are fairly rigid and physically resistant cells but the advent of sulphonamides and penicillin has shown systemic bacterial infections to be vulnerable to successful chemotherapeutic attack. The work of Browning and his collaborators on the acridine antiseptics was a feature of the 1914–1918 war and further vigorous study by Albert and his colleagues (1945) in Sydney has extended our knowledge of this field. The use of the quinine derivative optochin in the chemotherapy of pneumococcal septicaemia in mice (Morgenroth & Levy, 1911), however, was the only known example of the cure of a generalized invasive bacterial infection prior to the introduction by Domagk of the sulphonamides. Modelling their work on Eisenberg's (1913) examination of the antibacterial action of azo-compounds in vitro and on the well-known azo-pyridine urinary antiseptics (Hörlein, 1935–6), Mietzsch and Klarer decided to use the azo-benzene molecule as a versatile carrier of substituents, the general method of synthesis being diazotization of an aromatic amine and coupling with another component. Klarer (1943) has given a clear account of the plan of campaign which helps one to understand in some measure the mental reserve which the german workers showed at first to the idea that prontosil (XXVII) was broken down in the body to give sulphanilamide (XXVIII), the substance responsible for the systemic antibacterial activity of the original dye (Tréfouël, Tréfouël, Nitti & Bovet, 1935). Following the lead set in the May and Baker laboratories, the introduction of heterocyclic radicals into the sulphonamide group led in succession to sulphapyridine (XXIX), sulphathiazole and the sulphapyrimidines of increasing efficacy and diminished toxicity, and the maximum degree of efficiency in this group appears to have been reached in the pyrimidine derivatives. The medical uses of the sulphonamides, as well as their limitations, are well known and require no elaboration here, except to remark that their "spectrum" of activity is largely confined to gram-positive aerobic organisms.



XXVII XXVIII XXIX

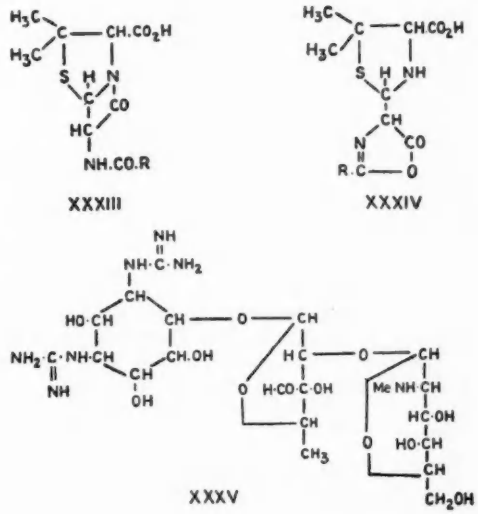
It was found by Klarer (1941) and Domagk (1942) that interposing a methylene group between the aromatic amino group of sulphanilamide and the benzene ring markedly modified the antibacterial "spectrum" and increased greatly the action of the sulphonamide type of drug on anaerobic organisms of the *Clostridium* group; the resulting drug, marfanil (XXX) hydrochloride, came into wide use in the german army for the prophylactic treatment of wounds. Approaching from an entirely different angle, Evans, Fuller & Walker (1944, 1945) showed that *p*-methylsulphonylbenzamidine (V187) (XXXI) and *p*-methylsulphonylbenzylamine (V335) (XXXII) hydrochlorides were similar to marfanil in their biological effects, and, unlike the case with the so-called "sulphonamides", the antibacterial action of these three drugs is not interfered with by *p*-aminobenzoic acid.



XXX XXXI XXXII

Antibiotics

Although knowledge of microbial antagonisms involving pathogenic organisms goes back to Pasteur, attention was only sharply focused upon this "unassuming commonplace of Nature" by Florey and Chain's successful development of the penicillin produced by Fleming's historic contaminant. The range of activity of penicillin among bacteria and spirochaetes and its lack of toxicity to the host alike distinguish it as the most remarkable chemotherapeutic agent yet discovered. On the chemical side it has proved one of the most tantalizing of natural products ever investigated. Degradation gave two readily recognized fragments, ββ-dimethylcysteine and an N-acylated-glycine derivative, but putting the pieces together again to give penicillin has been the alluring but discouraging task of numerous chemists for the past few years both in this country and in the USA. Only traces of antibacterial activity were detected in the products of synthesis and, even if du Vigneaud and his collaborators (1946) have isolated the substance responsible for the small degree of



XXXIII XXXIV XXXV

activity found and have shown it to be penicillin, the synthesis affords no unequivocal proof of structure. The unorthodox β-lactam structure (XXXIII) for the penicillins is considered to represent their structure more satisfactorily than the oxazolone-thiazolidine formula (XXXIV), R being different in different penicillins.

Chemical engineering has accomplished a remarkably fine feat in the large-scale production of penicillin, coping, as it has had to do, with the necessity for working under sterile conditions, with the labile nature of penicillin, and with the necessity for training personnel in methods hitherto unknown on such a scale. Of other antibiotics, streptomycin is the only one which appears to have established itself as therapeutically of value, although gramicidin and tyrothricin have had a limited application in medicine. The chemical nature of streptomycin has been worked out in american laboratories but, considering the structural formula (XXXV) for streptomycin and that of the penicillins, the prognosis for ultimate preparation synthetically is even less bright than with the penicillins.

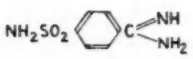
Present-day search among the metabolic products of moulds and other micro-organisms for therapeutic agents gives added interest to Samuel Butler's satire on a convert to Sir Kenelm Digby's[2] sympathetic therapy:

> Learned he was in med'c'nal lore,
> For by his side a pouch he wore,
> Replete with strange hermetic powder,
> That wounds nine miles point-blank would solder ;
> By skilful chymist, with great cost,
> Extracted from a rotten post ;
>
> *Hudibras*, Part I, Canto II.

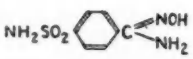
Chemotherapy of Rickettsial and Virus Infections

We have seen how the more-highly organized protozoal pathogens were the first to come under the control of chemotherapy and then later, descending the scale of biological differentiation, antibacterial chemotherapy became a practical reality. All these organisms, however, lead a free and independent existence and when we descend the scale still further to the rickettsiae of typhus and to the viruses we are dealing with parasites which are poorly endowed with synthetic abilities and which depend upon an intracellular environment for growth and multiplication. The position of the chemotherapy of rickettsial and virus infections has recently been assessed by Andrewes & King (1946) and by Findlay (1948), who have indicated the leads that are available. Andrewes and his colleagues (Andrewes, King, van den Ende & Walker, 1944; Andrewes, King & Walker, 1946) have shown that *p*-sulphonamidobenzamidine (V147) (XXXVI) and *p*-sulphonamidobenzamidoxime (V186) (XXXVII) hydrochlorides have a marked chemotherapeutic action in experimental typhus but human clinical trials, carried out in the wake of battle, were disappointing. A number of american workers have found massive doses of *p*-aminobenzoic acid to be of value in the treatment of some kindred diseases (Rocky Mountain spotted fever, scrub typhus) and dyes of the methylene-blue type have been studied experimentally with success. Penicillin, too, in massive doses has been reported as being active in experimental typhus.

[2] Sir Kenelm Digby (1603–1665), an iatrochemist, was one of the original Fellows of the Royal Society and a member of what is readily recognized today as the first National Committee for Chemistry.



XXXVI



XXXVII

Chemotherapy of Cancer

In cancer, chemotherapy has a problem which may well prove to be quite insuperable since the cancer cell, after all, is only a modification of the normal somatic cell, and " the conversion of a normal into a malignant cell is possibly brought about by a re-orientation of enzyme constitution of such a kind as would not necessarily involve any great change in gross protein-structure or in immunological specificity " (Haddow, 1947). On the other hand, the difference between sensitive and drug-resistant strains of the same species of bacteria can be similarly defined and we know that the appropriate drug will select and destroy the former strain, leaving the latter relatively unharmed. It has been suggested (Dubos, 1944) that certain gram-negative bacilli in their behaviour toward many types of antiseptics behave much more like animal-tissue cells than do other micro-organisms, and it may be that the chemotherapy of gram-negative infections will eventually suggest methods of approach to the chemotherapy of cancer.

On the practical side, which has been reviewed by Haddow (1947), it has been shown that oestrogens favourably influence cancer of the prostate, and there have been a number of studies of the effect of mitotic poisons on the growth of tumours. The specific cytotoxic effects of the chloroethylamine vesicants, which emerged from war-time biochemical study of these agents, suggested an investigation of their effects on malignant disease in man but it is still too soon to assess the results, and the same applies to the use of urethane in leukaemia.

Theories of Chemotherapy

Starting from the conception that all biological events are to be interpreted as chemical processes, Ehrlich postulated that " corpora non agunt nisi fixata " and considered that the ideal chemotherapeutic agent should be maximally parasitotropic and minimally organotropic, that is to say, it should have a great affinity for the protoplasm of the parasite and as little affinity as possible for the cells of the infected host. Although he realized that such absolute discrimination would not be possible as is the case in immunology where antibodies are exclusively parasitotropic and " nach Art von Zauberkugeln ihr Ziel selbst aufsuchen ", he set himself the ideal of a " therapia sterilisans magna " and sought a drug so powerful that one single treatment should kill all the infecting parasites in a treated host and leave the host unharmed. Ehrlich interpreted his results in terms of his side-chain theory and in terms of receptor groups on the parasites specific for functional groups in the molecules of chemotherapeutic drugs—cellular -SH groups, for example, being the receptors fixing arsenicals to susceptible trypanosomes. In anticipation of modern work, he clearly pictured the possibility of drugs hindering the uptake of essential metabolites and gave a " grobes Beispiel " in a letter to his cousin, Carl Weigert, in 1898 (see Heymann, 1928); his theory of " athrepsy ",

in fact, accommodates the idea of interference by a drug with a metabolic process. It is obvious, however, that ultimately, any antiseptic action results in the alteration of essential metabolic events.

Chemotherapy has remained essentially an experimental science and such theories as there are, and they are not many, have been evolved to explain observations and not to pave the way for fresh discoveries. This is scarcely surprising when one considers that the biochemistry, and particularly the enzymology, of micro-organisms is still, relatively speaking, in its infancy; the attack on the problem of bacterial nutrition through the analysis of complex empirical media only began to bear fruit little more than a decade ago (see Knight, 1945). Further impetus to theories of chemotherapy came when Woods (1940) showed that a substance isolated from yeast extracts capable of antagonizing the antibacterial action of sulphanilamide had properties recalling those of *p*-aminobenzoic acid, which itself has this anti-sulphanilamide activity. The great similarity in the formulae of sulphanilamide and *p*-aminobenzoic acid led Fildes (1940) to state with greater precision than anyone previously that a drug might interfere with an essential metabolite and so inhibit growth, and that it might do so in one of three ways, of which the most interesting was by competition for an enzyme associated with the essential metabolite. It was postulated that *p*-aminobenzoic acid, whose biological significance first came to light in this extremely indirect manner, was an essential metabolite for certain bacteria and that, in virtue of structural similarity, sulphanilamide, and, of course, sulphonamides generally, displaced it from its enzyme and thus stopped an essential line of metabolic events. Such an inhibition requires an inhibitor so closely related in chemical structure to the essential metabolite that it can fit the same enzyme and yet sufficiently unrelated to be devoid of essential metabolic activity. Further work has shown this simple sulphonamide—*p*-aminobenzoic-acid thesis to be an over-simplification (Henry, 1943, 1944) and, although Fildes suggested that other chemotherapeutic agents might be sought by modelling drugs on known essential metabolites, further intensive work (see Roblin, 1946) has so far failed to produce a single therapeutic agent of practical value, but the qualitative generality of the phenomenon is not in doubt. Although analogues of essential growth-factors frequently inhibit in vitro growth of bacteria, they fail to show any chemotherapeutic activity because the metabolites on which they are based are normal constituents of the body-fluids of animals.

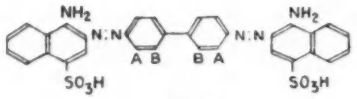
The discovery of *p*-aminobenzoic acid in a combined form in compounds of the folic-acid group, such as liver *Lactobacillus casei* factor (pteroylglutamic acid) (XXXVIII), was an event of considerable biochemical interest. There is evidence to show that many bacteria can synthesize folic acid (Sarett, 1947) and in some cases this has been related to the *p*-aminobenzoic acid content of the medium (Mayer, 1943; Mills *et al.* 1944). Recent findings also indicate that sulphonamides inhibit the synthesis of pteroic acid from *p*-aminobenzoic acid in the case of enterococci (Lampen & Jones, 1946). If O'Meara, McNally & Nelson (1944, 1947) are correct in their suggestion that reductone, CHO.C(OH):CH(OH), is the strongly-reducing non-sulphydryl substance found in bacterial cultures during the logarithmic phase of growth, it may well be that reductone provides the 3-carbon unit indicated in bold type in XXXVIII and that sulphonamides interfere with the synthesis of pteroic acid from *p*-aminobenzoic acid by competing with the latter for reductone, giving rise to biologically-inert analogues of pteroic acid (Forrest & Walker, 1948).

XXXVIII

Considerable success has attended the correlation of physicochemical properties of drugs with trends in the biological effects which they produce. For example, the experimental correlation of the acid dissociation constants of sulphonamides with in vitro antibacterial activity has shown that maximum activity is found in those drugs which are approximately 50% ionized at the pH of the medium considered (Bell & Roblin, 1942), the shape of the curve obtained on plotting these properties against each other indicating the operation of two factors; a plausible, but incomplete, explanation (Cowles, 1942) is that these drugs are absorbed in the undissociated form and that it is the ion which is active, although diaminodiphenyl sulphone and sulphaguanidine, which have no acidic properties, are embarrassing exceptions. Albert and his colleagues (1945) have shown that, among the aminoacridines, once a minimal degree of basic strength has been attained further increase does not influence antibacterial activity which has already reached a maximum, suggesting a simpler relation between activity and chemical constitution in this series than in the case of the sulphonamides; there is much to indicate that ion-exchange and acid-base neutralization phenomena form the basis of the biological effects of this and certain other groups of antibacterial agents.

The difficulties facing a theoretical approach to chemotherapy as a guide to synthetic operations by the organic chemist are well illustrated by the unfolding of events in the development of paludrine (XXIII). Had one of the suggested working hypotheses been followed unremittingly we might, for example, have had a number of extremely powerful antagonists of riboflavin, but we should not have had paludrine. Again, refined speculations in terms of the theory of resonance are of doubtful significance as a guide to the design of new drugs; it is noteworthy that the lower (methyl) homologue of paludrine, to which such considerations apply not one whit less than they do to paludrine itself, is not an antimalarial (Curd & Rose, 1946). Just as in the case of Bayer 205 where the two methyl groups (italicized in IV) are necessary for high biological activity and must occupy the positions shown and no others, so also with the lower homologue of paludrine, the two methyl groups which transform the methyl radical, $-CH_3$, into the *iso*propyl group, $-CH(CH_3)_2$, bring out the desired biological activity. One may take an illustration from another branch of applied chemistry where the participants are the cellulose fibre and three related dyestuffs. Congo-red (XXXIX, A and B being hydrogen atoms) has the power of dyeing cotton directly, although the colour is unstable to acids on account of the indicator nature of the dye. Substitution of two methyl groups at the two positions A,

giving benzopurpurin 4B, affords a similar substantive dye with increased stability to acid, but, on the other hand, similar substitution of methyls at the two positions B destroys substantivity altogether, the resulting dye showing no affinity for the cellulose fibre.



XXXIX

In their extensive study of trypanocidal dyes, Nicolle & Mesnil (1906) found that dis-azo dyes of the trypan-blue and trypan-violet type fell clearly into two classes, those that dyed cotton directly and those that did not; trypanocidal dyes fell in the first group and trypanocidal activity, as might be expected, was even more narrowly selective than substantivity. When simple chemical changes in molecules produce fundamental alterations in their behaviour towards the relatively simple and homogeneous cellulose fibre, it seems premature to theorize in terms of the much more complex living cell; in the ultimate analysis, the problem of biological specificity will yield only to experiment and not to argument.

Once the primary observation of biological activity is made on a new type of compound, (and this, of necessity, must be made empirically), the synthetic organic chemist is usually able, in the exercise of his craft, to provide a variety of related types. From the body of circumstantial evidence regarding structure and activity which grows thereby, it is possible with consequent economy of effort to narrow the search for maximum biological activity. In this cursory review of chemotherapy no reference has been made to the participation of the host but it goes without saying that, whether the chemotherapeutic agent acts directly on the infecting parasites or indirectly through a blockade of some kind, the final act in the recovery process is performed by the body, which may or may not have been an active participant in earlier stages as well.

It is only as our knowledge of the biochemistry of microorganisms grows that we may expect to reach a fuller understanding of chemotherapeutic processes and that the gaps in chemotherapy may be filled in. If we long ago abandoned the use of Ehrlich's nomenclature with its multiplicity of receptors, we must, at least, look upon it with indulgence, for, as Dale (1923) has pointed out, " Ehrlich's theory will always deserve the credit of having provided a vigorous stimulus to the investigation of problems which, without some kind of working hypothesis, might well have seemed beyond the reach of experimental attack ". The intervening years have given us a wide variety of new drugs and control over an ever-increasing number of pathogenic organisms. None of our chemotherapeutic agents, however, is so good as to be incapable of improvement and we must continue to seek for better ones, with enhanced margins of safety and presenting greater convenience in administration. Of penicillin we can entertain no criticism of its remarkable powers as a drug but its production is extravagant in man-power and material, and so the search for new synthetic antibacterial agents will go on, using penicillin as the yard-stick by which the newer drugs are measured. It may be that the chemotherapy of gram-negative infections will be suddenly opened up by a discovery matching the introduction of the sulphonamides, and there are signs that the practical chemotherapy of tuberculosis may not be long delayed. The fruitful collaboration of chemistry and medicine, which has given the physician the power to control with certainty infections which only a decade ago would have proved fatal, gives one a feeling of sober confidence that yet more benefits to humanity will accrue from their continued association.

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Continued at foot of page 369

SOME MEDICAL CONTRIBUTORS TO CHEMISTRY

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The debt of medicine to chemistry is well known, and one is constantly reminded of it by accounts of new drugs and anaesthetics, new materials for the construction of medical instruments and equipment, new knowledge of the processes that occur in living cells, and in many other ways. It is, however, much less generally appreciated that chemistry owes a very considerable debt to medicine, for many chemical discoveries of fundamental importance have been made by men whose academic qualification was the M.D. degree and many of whom carried on their chemical investigations while actively practising the profession of medicine. The occasion of the Chemical Society's recent centenary celebrations is an appropriate time to review this subject, for of the seventy-seven original members of the Society no less than fifteen were medical men.

For many centuries science and medicine were so closely interwoven that, especially among the humbler practitioners, it is now often impossible to distinguish one from the other. A slight acquaintance with contemporary knowledge of natural phenomena was frequently sufficient to establish a reputation as a healer; the term physician did not necessarily connote any specific qualifications and it was only in the higher ranks of the medical profession that any sort of control was enforced. The universities granted medical degrees from a very early stage in their history, and after 1518, when the Royal College of Physicians was founded, physicians practising within seven miles of London had to have the M.D. degree of the universities of Oxford or Cambridge. In England, membership of the Barber-Surgeons' Company or of the Society of Apothecaries became recognized as a definite professional qualification and similar professional organizations were established in other countries. The Barber-Surgeons' Company was formed in London in 1308 and the connexion between barbers and surgeons was not dissolved until 1745, when the College of Surgeons was formed and it was ordained that " no person using any shavery or barbery in London shall occupy any surgery, letting of blood, or other matter, except only drawing of teeth." The Apothecaries were formerly associated with the Grocers but they formed a separate Company in 1617. It will be seen therefore that in England an organized profession of medicine scarcely existed before the fourteenth century, when chemistry was still at the alchemical stage. Not until the sixteenth century did chemistry appear in anything like its modern form.

Paracelsus and his Successors

The first great figure linking chemistry with medicine after the alchemical era was Paracelsus (1493–1541), physician to the city of Basle. Among his many remarkable and sometimes unattractive characteristics was a profound contempt for authority. He used his own authority to order the destruction of existing medical and alchemical textbooks and placed his own views in their place. His greatest contribution to chemistry was his proclamation that the transmutation of base metals into gold must not be

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HISTORY OF CHEMOTHERAPY

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the sole aim of chemical experiments, though he believed that transmutation was a possibility. He taught that for the treatment of disease the pure substances produced by chemical methods were preferable to the empirical and often noxious brews then in common use. Paracelsus introduced many inorganic substances—including compounds of mercury, lead, sulphur, iron, arsenic, and copper—into general medical practice and was thus the founder of medical chemistry, or iatrochemistry as it is called.

Among medical men Paracelsus had several worthy successors to continue his iatrochemical doctrines. Angelo Sala (1575–1640) was physician to the Duke of Mecklenburg and also a chemist of repute. His *Opera medico-chemica* was published in 1647. Among his contributions to chemistry may be mentioned a clear description of ammonia and ammonium chloride and the preparation of nitric acid by the action of sulphuric acid on saltpetre. He was described by Conring as " the first chemist who ceased from trifling."

Another of the great iatrochemists was Johan van Helmont (1577–1644). Although he came of a noble family, and had estates in Brabant, he chose to give all his property to his sister and to devote himself to serious study. He took his M.D. degree in 1599. Thereafter he turned his attention to almost every branch of the arts and science and made several notable discoveries in chemistry. Perhaps his greatest achievement was his recognition of the nature of gases and his demonstration that there are several different kinds of gases. Earlier chemists had almost entirely ignored the gaseous products of their experiments, no doubt because of the difficulty of handling them with the apparatus at their disposal. Geber, for example, in describing an experiment in which ammonia is evolved, merely states that the nose should be averted from the reaction vessel. Van Helmont prepared carbon dioxide (rediscovered by Black in the eighteenth century as " fixed air ") by the action of acid on marble. He distinguished between gases and vapours. He introduced the use of the temperatures of freezing and boiling of water as fixed thermometric points. More important still, he emphasized the importance of the balance in chemical research. Although he never freed himself entirely from the ideas of the alchemists, and devoted a great deal of time to a search for the universal solvent or alcahest, van Helmont was a shrewd and careful observer and certainly one of the greatest chemists of his day.

Iatrochemists of the XVII Century

Among others of the early iatrochemists may be mentioned Oswald Croll (1580–1609), who was physician to Prince Christian of Anhalt Bernberg. He was responsible for the introduction into medicine of succinic acid, potassium sulphate, antimonic acid, calomel, and silver chloride. Guerner Rolfinck (1599–1673) was a physician with very catholic interests in science. He was successively professor of Anatomy, Surgery, Botany, Practical Medicine, and Chemistry at Jena; this is perhaps an unequalled record of academic versatility. According to Stahl, Rolfinck was responsible for having " brought chemistry into shape, deduced its operations from causes conformed into Nature and reason, and laid a foundation on which many subsequently built." Adrian von Mynsicht (1603–1638) practised medicine at Helmstadt. He discovered tartaric acid and used antimony sulphide and cream of tartar for the preparation of tartar emetic. François de la Boë, better known as Franciscus Sylvius (1614–1672), a disciple of van Helmont, practised medicine at Amsterdam. At his instigation the first chemical laboratory in Europe was built at Leyden, where he was professor of chemistry. He added considerably to knowledge of salts and their formation. Thomas Willis (1621–1675), the great authority on the anatomy of the nervous system, was also an able chemist. After graduating at Christ Church, Oxford, he practised in London. He investigated the preparation of ether and succinic acid.

John Mayow (1643–1679) was a doctor of laws of Oxford University. He practised medicine in Oxford and in Bath, though he does not seem ever to have gained the M.D. degree. He was in a sense the discoverer of oxygen, " officially " discovered independently by Priestley and Scheele a century later, for he recognized that there is a constituent of air which is concerned with both combustion and respiration.

In the year after van Helmont's death another great iatrochemist was born. He was Nicholas Lémery (1645–1715), who became a doctor of medicine of the University of Caen. Lémery's chemical lectures at his laboratory in the Rue Galande in Paris attracted not only the cream of french society but also numerous students from the whole of Europe. His textbook of chemistry, *Cours de chymie*, published in 1675, was a great success. It passed through thirteen editions in his own lifetime and remained a standard work for more than a century. Lémery was a fine experimentalist and his work did a great deal to clarify contemporary ideas on the preparation and properties of many compounds. He distinguished between organic and inorganic substances. Like van Helmont he appreciated the use of the balance and noted the increase in weight which occurs when lead and certain other substances are calcined. Although he found it difficult to reconcile this with the phlogiston theory he did not understand the real nature of combustion. While in Paris, Lémery is said to have made a handsome living by selling a cosmetic—" le seul Magistere de Bismut "—which was apparently a form of bismuth oxychloride.

Stahl and the Phlogiston Theory

Georg Stahl (1660–1734) is notable for having developed the phlogiston theory of combustion, postulated originally by Becher. Although the phlogiston theory proved false when subjected to the test of experiment it was in fact a good theory, and its use as a working hypothesis considerably advanced chemical knowledge. Indeed, it was in effect a negative expression of the correct theory of combustion, for the phlogiston theory becomes intelligible if, for the word phlogiston, we substitute " absence of oxygen." Stahl was a graduate of Jena who became professor of medicine at Jena and later physician to the King of Prussia.

Although Lémery had distinguished between organic and inorganic compounds, Hermann Boerhaave (1668–1738), a dutch physician, is generally recognized as the founder of organic chemistry. He was professor of medicine and botany, and later professor of chemistry, at the University of Leyden. His *Elementia chemiae* was published in 1724.

The glass and optical industries owe a considerable debt to John Bevis (1693–1771), a London physician who was the first to make glass with borax. He noted that this gave a glass with a high refractive index and thus pointed the way to the achromatic combinations which were developed many years later.

Scottish Pioneers

Another physician who made great contributions to chemistry, and founded the famous scottish school of chemistry, was William Cullen (1710–1790). He began his medical career as a ship's surgeon and later became an apothecary's assistant in London. He then practised as a surgeon at Hamilton, Lanarkshire, taking his M.D. degree at Glasgow in 1740. In 1756 he was appointed professor of chemistry at Edinburgh. Among his contributions to chemistry was the discovery that liquids become cold when they evaporate and when certain substances are dissolved in them. Pre-eminent among Cullen's many distinguished pupils was Joseph Black (1728–1799). Black took his M.D. degree in 1754, submitting a chemical thesis, *De humore acido a cibis orto et magnesia alba*, for examination. Black's work on the relationship between carbon dioxide and the oxides and carbonates of magnesium and calcium considerably clarified contemporary ideas on the nature of chemical combination and also emphasized the importance of quantitative work. He developed Cullen's work on latent heat and his work in this field led to Watt's construction of steam engines. Besides carrying out his extensive chemical investigations, Black found time to look after a large general practice in Glasgow. He was the first to hold the position of Physician to His Majesty in Scotland.

Although the work of the italian physician Luigi Galvani (1737–1798) was primarily in the physical field, it had nevertheless a considerable influence on the development of physical chemistry. His discoveries formed the background to the electrochemical researches of Michael Faraday, which in turn led on to an understanding of the process of electrolytic dissociation. Hermann von Helmholtz (1821–1894) has a similar claim to consideration. After a short career as an army surgeon he became professor of physiology at Königsberg, Bonn, and Heidelberg successively, but in 1871 his physical researches gained for him an appointment as professor of physics in Berlin. His discoveries—exemplified by his enunciation in 1847 of the conservation of energy in closed systems and the Gibbs-Helmholtz equation relating to chemical reactions—have materially advanced the progress of chemistry. In the same class, too, is Julius Mayer (1814–1878) who, like Cullen, began his career as a ship's surgeon, later taking up a medical appointment in his native town of Heilbronn. He was the first to calculate the mechanical equivalent of heat, a constant of great importance in physical chemistry. Mayer is reputed to have conceived his work on the mechanical equivalent of heat while on a voyage to the East Indies. While in the tropics he had occasion to bleed several members of the crew and he was struck by the unusual redness of their blood, indicating a low consumption of oxygen. From this he was led to consideration of the energy released in the metabolism of food and thence to determination of the mechanical equivalent of heat.

Carl Scheele: The XVIII Century

The swedish apothecary Carl Scheele (1742–1786) was responsible for discovering many new chemical substances. The long list of these includes arsenic acid, hydrogen sulphide, arsenic sulphide, chlorine, hydrofluoric acid, and lactic, oxalic, citric, and tartaric acids. He also carried out an extensive investigation of the properties of manganese. He anticipated Priestley in the discovery of oxygen and came close to discovering the nature of combustion.

Work on the study of gases was advanced by Daniel Rutherford (1749–1819), whose thesis for the M.D. degree at Edinburgh defined the difference between carbon dioxide and nitrogen. The acceptance of a chemical subject for the M.D. degree again emphasizes the close connexion that then existed between medicine and chemistry. Rutherford was the first to prepare nitrogen, which he obtained by removing oxygen from air by combustion. Priestley independently obtained nitrogen at about the same time and —a sign of his lifelong adherence to the phlogiston theory—called it " dephlogisticated air."

Another important figure in the chemical life of the late eighteenth century was Thomas Beddoes (1760–1808). He obtained his M.D. degree at Oxford and afterwards became University Reader in Chemistry. Subsequently he founded the Pneumatic Institute at Clifton, Bristol, primarily with the intention of studying the possible therapeutic effects of inhaling gases. As his assistant he engaged the young Humphry Davy (1778–1829), who at that time was proposing to go to Edinburgh to study medicine. Davy became so absorbed, however, in his chemical work at Bristol—where his discoveries included that of the anaesthetic properties of nitrous oxide—that he eventually abandoned his original intention of qualifying in medicine. Lyon Playfair (1818–1898) was another great chemist who began his career with the intention of qualifying in medicine, an intention which he was forced to give up owing to a breakdown in his health.

A great part of our knowledge of the chemical properties of platinum, and the discovery of a satisfactory method of rendering the metal malleable, is due to William Hyde Wollaston (1766–1828). He graduated as an M.D. at Cambridge and from 1789 to 1800 carried on general practice in various places, finally settling in London. He then abandoned medicine for chemistry and within a few years his mastery of the intractable metal platinum won him a fortune of £30,000. He discovered also the metals rhodium and palladium.

In this catalogue of medical contributors to chemistry, brief mention might perhaps be made of Alexander Marcet (1770–1822), less because of his activities in the field of pure chemistry—where his chief service was in teaching—than because his wife, with his collaboration, did so much to interpret chemistry to the general public. The first of her popular science books, *Conversations in chemistry*, had enormous sales throughout Europe.

Among the greatest chemical figures of the early nineteenth century was Jons Berzelius (1779–1848), a Swede who graduated in medicine at Uppsala in 1802. From 1807 onwards he taught medicine and pharmacy at Stockholm, adding chemistry to his course in 1815. It is as a chemist that he is remembered. Among the impressive

list of his achievements in chemistry may be recalled his long series of determinations of atomic weights, his experiments in electrolysis, his discovery of selenium, cerium, and thorium, his isolation of columbium and silicon, his introduction of the modern system of chemical symbols, his improvement of analytical methods, and his classification of minerals according to their chemical constitution.

The work of William Prout (1785–1850) on the determination of atomic weights by vapour density measurements, of which he published an anonymous account in 1815, proved of value in clarifying some of the uncertainties about atomic weights which existed in the early nineteenth century. His famous hypothesis—that all atoms are made up of hydrogen atoms and that the atomic weights are therefore very nearly whole numbers—proved incapable of substantiation at the time, but the discovery of isotopes nearly a century later showed that his idea had in fact some substance. Prout was a Gloucestershire man who qualified in medicine at Edinburgh and practised in London.

Although recent study of the contemporary literature tends to diminish the significance which has been attached to his conversion of inorganic ammonium cyanate into organic urea, the chemical researches of Friedrich Wöhler (1800–1882) are well worthy of notice in other respects. His isolation of aluminium in 1827 and of beryllium in 1828 are of particular interest. He also devised a method for manufacturing nickel and carried out important investigations on the phenomenon of isomerism.

Some Irish Chemists

Among irish chemists of the nineteenth century Sir Robert Kane (1809–1890) was pre-eminent. At the age of thirty-five he had established a european reputation as a chemist but, unfortunately for chemistry, he was also an able administrator and educationist and as such attracted the attention of Sir Robert Peel, who induced him to take up political work. After qualifying in medicine Kane went to Paris to study pharmacy in 1830. In the following year he was appointed professor of chemistry at Apothecaries' Hall, Dublin. In the same year, at the remarkably early age of twenty-two, he was elected to the Royal Irish Academy. Among his chemical discoveries may be mentioned the synthesis of mesitylene from acetone, the recognition of the ethyl radical, the use of calcium chloride in the purification of methanol, his researches on archil and litmus, and the investigation of mineral manganese arsenide, which was subsequently named Kaneite in his honour. He was a gifted writer and his textbook of chemistry was regarded as the best of its day. In the political field, another book, *The industrial resources of Ireland*, created an equally great impression. He was the founder of the *Dublin Journal of Medical and Chemical Science*, which is still published in the form of a purely medical journal with the title of *The Irish Journal of Medical Science*.

Another distinguished Irishman of the same period was Thomas Andrews (1813–1885), who took his M.D. degree at Edinburgh in 1835. After practising for a time in Belfast he was elected professor of chemistry in Queen's College, Belfast, in 1849, and held this post for thirty years. Andrews is best known for his important work on the liquefaction of gases and his discovery of the existence of critical temperatures and pressures.

The Chemical Society Founded

Among the great chemical problems of the early and middle nineteenth century was that of discovering how atoms are linked together to form molecules. For our modern conception of valency much is owed to Friedrich Kekulé, who was for a time a lecturer in chemistry at St. Bartholomew's Hospital, London, but many outstanding problems were clarified by the work of William Odling (1829–1921). Odling qualified in medicine in 1851 and then went to Paris to study chemistry. On his return to England he was engaged in laboratory work and in lecturing on chemistry at Guy's Hospital. In 1868 he succeeded Faraday as Fullerian Professor of Chemistry at the Royal Institution. Later he succeeded Brodie in the Waynflete Chair of Chemistry at Oxford and did not retire from his long life of active chemical work until 1912.

Odling was among the last of the great chemists whose academic qualification was a medical degree. By the middle of the nineteenth century, facilities for the teaching and practice of chemistry and for the exchange of information had become sufficient to meet the rapidly growing interest in the subject without dependence upon the medical profession. The most significant event in this respect was the foundation of the Chemical Society in 1841, for the meetings and publications of the Society proved an excellent medium for the discussion of controversial chemical subjects and the exchange of information. In 1845 the Royal College of Chemistry was founded in London, with W. A. von Hofmann as its first professor. The first university chemical laboratory was opened in Oxford in 1854 and at Cambridge in 1887, though at both Universities chemistry had been taught for some two hundred years previously. A school of chemistry was formed in Manchester in 1851. Adequate training thus became available to all potential chemists, without need to take the medical course.

Medical contributions to chemistry still continue, however, though in a rather different way. Collaboration between physician and chemist, the one venturing some distance into the now vast field of chemical knowledge and the other essaying to master some knowledge of medicine, has proved of great advantage to both, particularly in the study of physiologically-active substances such as antibiotics, vitamins, hormones, and carcinogens.

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TYPHUS AND CHEMOTHERAPY

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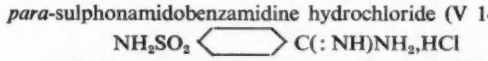
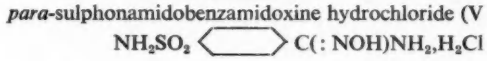
This report[1] covers a large part of the work on typhus carried out between 1941 and 1946 at the National Institute for Medical Research, Hampstead, London, and at the Royal Army Medical College Emergency Vaccine Laboratory, Everleigh, Wilts. Publication of many aspects of the work had been withheld for security reasons. The largest part of the report is concerned with observations made during clinical trials of two drugs, in North Africa and Italy. These substances h: 1 given highly promising results in laboratory tests recorded in 1944 by Andrewes, King, van den Ende & Walker. The two substances were:

para-sulphonamidobenzamidine hydrochloride (V 147)



para-sulphonamidobenzamidoxine hydrochloride (V 186)



Toxicity of V 147 and V 186

The results of toxicity tests in mice, guineapigs, rabbits, rhesus monkeys and man are recorded in the first section by C. H. Andrewes, A. M. Begg & M. van den Ende. The maximum daily dose in g./kg. tolerated *per os* over several days was greater for mice (2) than for rhesus monkeys (0.25) or guineapigs (0.3). A daily dose of 0.13 g./kg. was tolerated by human volunteers without ill-effects.

Chemotherapeutic Trials

Section II, comprising 118 pages, is a report by the British Army Typhus Research Team on chemotherapeutic trials in typhus fever in man and a report of the 1943–4 Naples typhus epidemic. The team began work in Algiers in July 1943 and although the number of cases available throughout the summer and autumn was small the experience gained was valuable. It was established that the drug V 186 did not produce an obvious clinical effect when given to patients in the second week of the disease. The cases were mostly in Arabs under the age of 40, with a gross mortality from typhus of only 11 per cent. Only one-third of the cases was admitted before the 8th day of the disease. If the diagnosis of typhus seemed likely on clinical and pathological grounds, alternate patients were given V 186. Of the entire group of 65 patients investigated, a final diagnosis of typhus was made in 21, other diagnoses being established in the remainder on the basis of clinical examination and extensive laboratory investigations. Details of clinical course and laboratory findings are given in respect of the typhus patients. It was felt that V 186 did possibly cause a slow amelioration of the disease but the need for further observations on a large group of patients was obvious. One patient apparently developed kidney damage, either because of the effect of the drug alone, or because of the combined effect of the drug and the lesions of typhus.

The Naples Typhus Epidemic 1943-4

The Naples outbreak developed in December 1943 and much of the work was transferred to that centre. The chemotherapeutic trial of V 186 was made on new cases admitted to hospital between 2 January and 9 February 1944, the period which included the time of maximal prevalence of typhus in the city (913 cases were reported during January). The American Typhus Commission was very active and co-operative. An analysis of the cases from December 1943—February 1944 showed that the mortality among 1423 cases was 13.9 per cent. There were however 12 deaths among the 50 control cases admitted to hospital and forming part of the trial. A detailed analysis of the clinical course, symptomatology, and physical findings in these cases is presented and tabulated. Similar data are given for 30 patients in the "treated" group: of these, 27 received V 186 and 3, V 147. In the final comparison of the 30 patients in the treated group with the corresponding 30 controls there were 8 in each group classified as severe and, of these, 7 in the treated group died and 5 of the controls. The two groups had been reasonably comparable in duration of illness prior to admission, in age and sex incidence and in symptomatology. In those who recovered there was no difference between the two groups in the duration of fever after admission to hospital. In considering possible toxic effects, vomiting was more frequent in the treated patients and in five a peculiar collapse or shock-like state occurred. There was clinical evidence that V 186 was probably exerting a toxic action on the kidney and in fatal cases severe tubular degeneration of the kidney was found. Penicillin was given to a few of the control cases but did not exert any marked beneficial effect on the course of the disease.

The results of pathological investigations carried out are given in some detail: strains of rickettsiae were isolated from 17 patients by inoculation of blood into guineapigs, and 11 were adapted to mouse lungs. Three attempts were made to isolate rickettsiae from the blood of patients who had been treated with V 186 for 24 hours or more, and all succeeded. Useful data are given on the development of agglutinins for murine and epidemic rickettsia and for *Proteus OX19* and *OX2* in 59 patients. Complement-fixation tests made on some of the sera against freshly prepared rickettsial suspensions gave positive results with epidemic, but negative with murine, antigens. The findings in relation to blood-counts and blood-chemistry are discussed and the morbid anatomy and histology, based on 24 autopsies, is described. As indicated above, tubular degeneration in the kidneys was much more severe in the treated than in the control series.

The reason for the failure of V 186 in the treatment of typhus in man and its success in the mouse is not quite clear and it is suggested that the elucidation of this difference might serve to explain the mode of action of the drug.

[1] [For particulars see Book Reviews.]

Test for Neutralizing Power of Antirickettsial Sera

In section III, by M. van den Ende & K. C. Mills, experiments on a quantitative test for neutralizing antibodies against typhus rickettsiae are described. The method depends on the determination of the extent of the reduction in the number of focal lesions produced in the lungs of mice inoculated intranasally with rickettsial suspension mixed with progressive dilutions of serum. The inhibitory effect of serum was not noticeably increased by prolonging the contact of serum and rickettsiae for more than half-an-hour before inoculation into mice. The test gave fairly accurate results with sera which were sufficiently potent to reduce the focal-lesion count to 20 per cent., or less, of that in the controls. Many human sera studied, however, were not of this potency. With immune rabbit-sera against epidemic strains, neutralization of murine rickettsiae was poor compared to that against homologous rickettsiae. The reduction in the focal-lesion count was not dependent on the agglutination of rickettsiae. The mouse test gave more satisfactory results than the Giroud test of neutralization by intradermal injection of serum-rickettsiae mixtures into rabbits.

Comparison of Typhus Vaccines

Section IV, by F. Fulton, M. van den Ende, W. J. Elford & K. C. Mills, is devoted to a study of laboratory methods for comparing the potency of typhus vaccines. The methods of preparation of four murine vaccines, two from yolk-sacs (A and B) and two from mouse lungs (C and D) of approximately equal rickettsial content, are described. Two of the vaccines were highly purified, one (A) from the yolk-sac by Craigie's ether method, the other (B) from mouse lung by the kieselguhr method which, in its improved form, is described in detail in the succeeding section. Photomicrographs of representative fields of the four vaccine-suspensions are reproduced on plate X. The vaccines were standardized after the number of rickettsiae present had been estimated by the microscopical examination of stained films. The potency of the vaccines was compared by: (*a*) active immunization of guineapigs by one intraperitoneal injection of vaccine; the animals were tested 37 days later by intraperitoneal injection of a yolk-sac suspension of living rickettsiae; (*b*) protection of mice by a single dose of vaccine against the toxic effect of a certainly fatal dose of rickettsiae injected intravenously; and (*c*) by the production of antibodies in vaccinated rabbits and guineapigs. The rabbits received three doses of vaccine intravenously at four-day intervals. The guineapigs were those used in method (*a*) and were bled for serum before the challenge dose of living rickettsiae was injected. The antibodies studied in sera of immunized rabbits and guineapigs were: rickettsial agglutinins, agglutinins for *Proteus OX19*, complement fixing antibodies, "antitoxins", and neutralizing antibodies. The titres of antibodies were lower in the guineapig sera than in the rabbit sera. *Proteus OX19* agglutinins were present in the rabbit sera only in small amounts—highest titre 1/40—and were not tested in the guineapig sera. By these methods, no significant difference in the antigenic potency of the four vaccines was detected and it is concluded that potency depends on the number of rickettsiae present and is independent of the soluble antigen. The power of a vaccine to protect mice against the toxicity of rickettsiae injected intravenously affords the most convenient and reliable test for vaccine potency.

Antigenic Structure of Typhus Rickettsiae

In section V (29 pages), a detailed serological study of the antigenic structure of typhus rickettsiae by F. Fulton & A. M. Begg is presented. The Wilmington murine strain and a Cairo epidemic strain (isolated in 1942) were used in most of the work. Immune rabbit- and guineapig-sera were obtained from animals after a single intraperitoneal infecting-dose of rickettsiae from yolk-sacs or mouse lungs. For some of the later experiments rabbits were immunized by intravenous injection of *Proteus OX19* suspension or by repeated intravenous injections of various rickettsial antigens. Agglutination tests and the complement-fixation reaction were used throughout. Purified suspensions for agglutination tests and for absorption of sera were prepared from rat- (murine strain) or mouse-lungs. Antigens for complement fixation were prepared in the same way, although yolk-sac antigens were also used in the experiments on soluble antigen. The working hypothesis adopted by the authors was based on the propositions: (i) that the antibodies formed in response to one antigen are not entirely uniform but vary in specificity to some degree, and (ii) that the heating of some antigens to 100°C. creates a new antigenic specificity.

From the results of their carefully-planned experiments with unabsorbed and absorbed sera, the authors reach the following conclusions: the surface antigen of the murine strain of typhus rickettsiae is similar to, but not identical with, the surface antigen of the epidemic strain; the murine rickettsial surface-antigen gives rise to a heterogeneous group of antibodies, some of which can react with the surface antigen of the epidemic strains; similarly the epidemic surface-antigen gives rise to antibodies, some of which react with the murine surface-antigen.

Boiling a rickettsial suspension so alters the surface antigen that it acquires a new serological specificity. Such degraded antigens have lost their strain-specificity. Rabbit and guineapig rickettsial antisera contain an antibody which reacts with boiled rickettsiae but this antibody is entirely distinct from the antibody which reacts with the undegraded rickettsiae. The *OX19* antibody of rabbit rickettsial antisera is entirely distinct from the antibodies to the undegraded surface-antigen of the rickettsiae, but it is a fraction of the group of antibodies which reacts with the boiled rickettsiae. Shaking a rickettsial suspension with ethyl ether provokes the release into the surrounding fluid of a soluble antigen which behaves as if it were a fragment of the surface antigen, though there is evidence that it is partially degraded.

Case Reports and Drugs Tested

In appendix A (50 pages) are set out summarized reports of 13 representative cases which illustrate the respective features of severe, moderate and mild typhus treated with or without chemotherapy. An account of the postmortem findings and histology is given with the reports of the six fatal cases. Some of the histological lesions found in typhus cases are illustrated by excellent photomicrographs on plates II–IX. A second appendix gives a list of the

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FACTOR ANALYSIS IN PSYCHOLOGICAL MEDICINE

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The application of statistical methods to problems of psychiatry is of quite recent origin. Yet it promises to throw a new and revealing light on many unsolved problems.

The idea of disentangling contributory causes by means of a statistical analysis is due to Galton. The fundamental technique is the calculation of a coefficient of correlation, which was intended to assess the relative importance of a common cause or factor by measuring the amount of agreement between its effects: it was used, for example, to measure the influence of inheritance in a physical characteristic, such as stature. Later, Galton was led to study the concomitant variation of a number of characteristics considered as a group. Thus, in discussing Bertillon's scheme of physical measurements for the identification of criminals, he pointed out that what was really needed was a set of traits showing as little intercorrelation as possible. Pearson carried this argument to its logical conclusion; and showed how the variations of a large number of intercorrelated characteristics might be described in terms of a small number of uncorrelated factors. Thus, in physical measurements, we find a "general factor" for size, accounting for the fact that growth in all directions is more or less proportionate, and a special or "bipolar factor" for body-build, accounting for the familiar classification of individual physique into the well-known leptomorphic and pachymorphic types (Kretschmer's asthenic and pyknic types).

The first psychologists to use correlational methods for the study of mental capacities were Galton's own pupil, McKeen Cattell, and Cattell's younger colleague Wissler. They assumed that, with mental traits as with physical, both general and special factors would be found. Spearman, however, made the startling suggestion that all the intercorrelations between mental characteristics could be attributed to one general factor only. Although his view is no longer accepted, the eager controversies that it aroused led to a vast number of factorial studies, mainly concerned with tests of intellectual abilities. Owing partly to the pressing needs of educational organization, and partly to the accessibility of children for mental testing, the greater part of this early pioneer work was carried out by educational psychologists, schoolteachers, and school medical officers, working in London schools. From a practical standpoint, the most important outcome was the demonstration of an innate, general, intellectual factor popularly known as "intelligence", and the development of standardized tests for the diagnosis of mental deficiency and for educational and vocational guidance generally.

The problems referred to the school psychologist, however, included not only cases of intellectual deficiency and special disabilities, but also cases of emotional or moral disorders—delinquency, psychoneurosis, and so-called moral deficiency. Here the problems of classification and causation were still more bewildering. Accordingly, as early as 1915, it was suggested that the factorial technique might be fruitfully applied to the investigation of the emotional aspects of human personality. Almost at once, a general factor of emotionality was clearly established, together with bipolar factors reminiscent of the old traditional temperaments. The former, it was suggested, indicated the element of truth contained in McDougall's notion of a "common fund of emotional energy" and Jung's later doctrine of *libido*. The latter provided a confirmation of Binet's distinction between "objective" and "subjective" types of personality, and the analogous distinctions between "extraverts" and "introverts" (or "cyclothymes" and "schizothymes") as suggested by Jung and Kretschmer. By 1923, factor analysis had provided a convenient working scheme for the study of what was called "personality",[1] which has been used freely in child-guidance clinics and elsewhere; and, what was even more important, the method made it possible to assess, with some approach to scientific accuracy, the relative importance of different contributory causes and of different diagnostic symptoms in various subnormal conditions.

During the last twenty years these statistical devices have been taken up with great enthusiasm in the USA under the lead of Kelly, Holzinger and Thurstone. The chief results are brought together by Dr. Raymond Cattell in his recent book, *The description and measurement of personality*.[2] The change in viewpoint will be seen at once on comparing this work with that of Gordon Allport on personality.[3] Allport's masterly review followed the

[1] Cf. C. Burt, Mental differences between individuals. *Rep. Brit. Ass.* 1923, p. 215.
[2] Raymond B. Cattell, *The description and measurement of personality*. New York, World Book Company, 1946; London, Harrap & Co.
[3] G. W. Allport, *Personality: a new psychological interpretation*. New York, 1937.

CHEMOTHERAPY IN TYPHUS

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numerous drugs tested in the laboratory for activity against typhus by Andrewes, King, van den Ende & Walker (1944).

Although the chemotherapeutic trials against typhus fever were not successful under the conditions in which they were carried out, the detailed clinical, biochemical, serological and pathological investigations made during the trials and reported in this monograph constitute a valuable record of louse-borne typhus as seen in North Africa and Naples in 1943 and 1944. The laboratory studies on the immunology of typhus fever, made at the National Institute for Medical Research and at the Royal Army Medical College Emergency Vaccine Laboratory, are an important contribution to knowledge in this field.

REFERENCE

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impressionistic studies of Jung, Freud, and Stern, and appeared before the wave of statistical researches on human personality had fully reached America. In his own survey, Dr. Cattell enumerates about thirty different factors, all apparently well established in the sense that they have been found by at least three independent observers. Many of these, however, seem to be different names, or allied forms, of much the same thing; and he believes it possible to reduce the entire list to about twelve fundamental components. To a large extent these correspond with the factors already discovered in Britain. They include general ability (or intelligence), certain special intellectual abilities, general emotionality, and a number of temperamental factors. Most of them have definite implications for psychiatric work; and some seem primarily concerned with clinical or abnormal states. Of these the most important and the most conspicuous is that making for a cyclothymic or schizothymic temperament; others make for melancholia, hysteria, neurasthenia, paranoia, anxiety, and their respective opposites.

Dr. Cattell's list of factors, as he himself emphasizes, is provisional only. But it is evident that, if this procedure is applied rigorously and systematically to further trustworthy data, it will do much to solve the puzzling problems of the classification of nervous and mental disorders. The accounts that are now being issued of the results obtained by psychologists and psychiatrists, both in Britain and in the USA, suggest that in two or three points his conclusions will need revision. He has evidently overrated the validity of behaviour-ratings and personality-tests as compared with personal questionnaires; he tends to describe normal characteristics in terms of psychiatric concepts rather than vice versa; and he is apt to force as many factors as possible into bipolar form. These defects, however, are defects rather of the material available at the time of his investigation than of Dr. Cattell's own standpoint.

A recent book, *The dimensions of personality** by Dr. Eysenck, carries the results still further. It records the results of more than three dozen separate researches carried out on several thousand normal and neurotic subjects, Most of the work was done at Mill Hill Emergency Hospital, and the majority of the patients were men and women referred from the Armed Forces. An important feature of the investigations has been the close collaboration between medically-qualified psychiatrists and a group of non-medical psychologists using such specialized techniques as standardized tests and factorial analysis.

The investigators " started from the position that measurement in the field of personality is impossible until the dimensions along which such measurement can take place are known." The field of survey has not been limited entirely to normal or abnormal traits of temperament, but covers bodily physique and constitution, intellectual ability and efficiency, aesthetic appreciation and expression, and problems of hypnosis and suggestibility. A separate chapter is devoted to each of these main topics. Much the same factors or dimensions are discovered as before; and the same " hierarchical view of the structure of personality " is in the main confirmed. In particular, the analysis of the data obtained from neurotic cases has fully corroborated two main factors—which (subject to certain reservations) are labelled " neuroticism " and " extraversion-introversion " (or " hysteria-dysthymia ").

Dr. Eysenck and his colleagues have discussed, in the light of their evidence, the value of physical types, physiological symptoms, and personality-tests for the diagnosis of psychoneurotic and psychotic disorders, and for the discrimination of the main subclasses. They frankly admit that their conclusions are tentative and sometimes even negative. That is almost inevitable in view of the material available. But their results demonstrate two points beyond all question: first, the value of co-operative research on common problems approached simultaneously from the standpoints of the psychiatrist and the psychologist respectively, and second, the value of testing tentative hypotheses and current views by an adequate statistical technique.

* [For particulars see Book Reviews.]

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Annotations & News

1212

SOME MEDICAL CONFERENCES

Among the medical conferences being held this summer we have received notice of the following:

In London. International Congress on Mental Health, Central Hall, Westminster; from August 11–21, 1948, under the presidency of Dr. J. R. Rees, C.B.E. The Congress will be in three main parts: (1) Child Psychiatry—Theme: Personality development with special reference to aggression (August 11–14, morning sessions); (2) Medical Psychotherapy—Theme: Guilt (August 11–14, afternoon sessions); (3) Mental Hygiene—Theme: Mental Health and World Citizenship (August 16–21). All enquiries should be addressed to The Congress Organizer, International Congress on Mental Health, 19 Manchester Street, London, W.1.

Under the auspices of the Commission Internationale Permanente pour la Médecine du Travail, the Ninth International Congress on Industrial Medicine—the first for 10 years—is being held at the Caxton Hall, London, S.W.1, from 13 to 17 September, 1948. The Congress will be in six sections dealing with Social Aspects, Environment, Nursing, Clinical, Practice, and Special Subjects. Visits to Rehabilitation Centres, Clinics, Hospitals, etc., during Congress week and the week following are being arranged. The address of the Organizing Secretary is Room 501, Garden Court Wing, BMA House, Tavistock Square, London, W.C.1.

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At Salzburg, the Austrian Medical Conference will be held on the 6, 7 and 8 September, 1948. The two main subjects of the Conference will be Blood Transfusion and Hypertension. Enquiries to the Sekretariat der oesterreichischen Aerztetagung, Salzburg, Landeskrankenhaus.

* * *

In Budapest, in connexion with the centenary celebrations of the Hungarian War of Liberty, 1848, the Hungarian Medical Trade Union is arranging a Medical Week from 4 to 12 September, 1948. Detailed programmes will be sent, on request to the General Secretary, the Hungarian Medical Trade Union, Budapest V, Nádor Utca 32.

* * *

Les Entretiens de Bichat 1948. In Paris the second annual series of informal discussions is to take place from the 10–17 October at the Hôpital Bichat. There will be two series of 100 discussions: (i) on surgery and various specialities (oto-rhinolaryngology, electro-radiology, gynaecology and obstetrics, ophthalmology, stomatology), from the 10–13 October, under the direction of Professor D. Petit-Dutaillis; (ii) on large questions of general modern medicine, from the 14–17 October, under Professors Guy Laroche and L. Justin Besançon.

The discussions are arranged in four series, each of 2 days, and are to be carried out with the help of 100 doctors from Paris hospitals, who are abreast of the latest clinical and therapeutic advances. Outlines of each subject will be supplied beforehand, and then discussed informally. Abstracts of all the introductory talks are to be published in September before the discussions by the Expansion Scientifique Française, 23 rue du Cherche-Midi, Paris.

Last year's colloquia, which were most successful, were attended by 842 french and foreign practitioners. Enrolments for 1948 can be sent to the Hôpital Bichat (Paris 18e).

1213

FRENCH WAR-TIME RESEARCHES

It is difficult enough for those who did not actually experience nazi occupation to imagine how ordinary life was carried on, under material and moral conditions which defy description. It is still more difficult to visualize the continuance of scientific research under such conditions. It was the resulting attitude of incredulity which struck Professor Pasteur Vallery-Radot on a post-war visit to America and gave him the idea of publishing a collection of articles which would be representative of the extensive and varied medical researches actually carried out in France during the war. This project, in which he enlisted the services of Professor Jean Hamburger, of the Paris Faculty of Medicine, has resulted in an impressive volume entitled *Recherches médicales en France pendant la guerre* (1939–1945)[1], and containing 30 articles. Many of these had already been published, in journals or as part of a book, but several were written specially for this collection. The variety of subjects is wide, ranging from the purely clinical, as in the articles by Debré, Marie, Seringue & Mande, "Remarks on a neuro-oedema syndrome" (p. 7) and Gutmann, "Initial signs of gastric cancer" (p. 53), to details of chemical and bacteriological research, as in the articles by Nitti, Tabone & Mousset on "The antisulphonamide activity of peptone" (p. 245) and Lépine on "Studies on the determination, by means of ultracentrifugation, of the size of bacteriophages" (p. 39). The authors mentioned are but a few of the eminent authorities included among the contributors. Other examples are: Leriche, "Remarks based on 800 lumbar ganglionectomies"; Lacassagne & Danysz, "Three notes on mammary cancer in mice" and two articles by Vallery-Radot and others on "Clinical and biological discussions of polycystic kidneys" and "Effect of sulphonamide therapy on the kidney".

The reader cannot help being impressed by this wide range of subjects and the wealth of detailed and careful investigation that has been carried out. The criticism that there is no evidence, in this haphazard collection of individual observations, of any planned research into particular fields, while true as an isolated statement, is surely one which ignores the conditions, described in Vallery-Radot's preface, under which the work was done, and which played such an important role in the genesis of the book. The expressed object of this volume is to show the outside world that, in spite of indifference, and even active opposition, from above, french scientific workers still "carried on" under the german occupation. In these circumstances, planned research would hardly have been possible, and the book aims merely at presenting representative samples of the work accomplished. A more valid argument would seem to be that the editors might well have arranged their material more systematically, grouping the articles by subject, even though the work described was actually done independently, instead of in an apparently arbitrary order. This would have been a great improvement from all points of view; it would have answered even more satisfactorily those sceptics who believed french scientific investigation to be at a standstill during the war, by showing at once how much had been done in each field; it would have facilitated reference; and lastly, it would have created a more orderly impression in an otherwise excellently produced book.

The physical composition of the book is of a high standard: paper and type are good; the half-tone illustrations (radiographs, etc.) leave something to be desired, but the tables and graphs are neat in appearance and, on the whole, clear. An attractive and useful feature is the brief summary at the beginning of each article, printed in italics and enclosed in a "box". Full bibliographies are appended to most articles, but it is a pity that no consistent style for references appears to have been used.

It would seem appropriate to say a special word on the subject of indexes. There is a list of contents in chronological (and therefore haphazard) order, but no index to this book. This exemplifies an all too frequent omission in french works, often, as in this case, lowering the generally high standard of production. In addition to a subject index, an alphabetical list of authors would be useful here.

In spite of these few criticisms, however, it seems to us, in the first place, an interesting and useful idea to publish a book of this kind and, in the second place, that the editors' aims have been, for the most part, fulfilled. The book cannot fail to impress its readers and will be a lasting tribute to the achievements of France in medical research under the occupation.

A. H.-S.

[1] [For particulars see *Book Reviews*.]

1214

ANTI-TUBERCULOSIS MEASURES IN SPAIN

Five books[1] issued during 1945, 1946 and 1947 by the *Patronato Nacional Antituberculosa*, which deal with tuberculosis control in Spain, have reached us. Two of these books are entitled *La lucha antituberculosa en España*, one being a book of 366 pages, published in 1945 and giving a detailed account of the activities of the *Patronata Nacional Antituberculosa* (PNA), its organization, administration and future plans. It includes statistical information on the results of investigations by PNA into the incidence of tuberculosis in Spain, and gives particulars of the services which have been set up to combat this disease. The second and smaller book was published in 1946 and gives a summary of the progress made by the PNA since its foundation in 1936 in the provision of services for tubercular patients. Many new sanatoria have been established and the number of beds available for tubercular patients has risen from 2,500 in 1936 to 11,000 in 1946. One of the preventive measures adopted by the PNA has been the establishment of settlements for children with a family history of tuberculosis. Both these books are illustrated with numerous photographs and tables.

The other three publications of the PNA deal with special aspects of the antituberculosis campaign. *La tuberculosis pulmonar inadvertida*, 1946, by Dr. Jose Zapatero stresses the importance of early *x*-ray diagnosis and gives details of radiological investigations carried out among various groups of the population such as soldiers, miners and students. Dr. Zapatero emphasizes the need for increased sanatorium accommodation. *Estudio de las contralateralizaciones, especialmente precoces, en los procesos pulmonares tuberculosos de apariencia radiológica unilateral*, 1946, by Dr. F. Tello-Valdivieso contains clinical histories of a number of his patients at the central antituberculosis dispensary in Zaragoza, and gives an account of their treatment and progress. The book is illustrated by numerous plates and includes a bibliography. *Estudios sobre el pulmón colapsado*, by Dr. Jose Abelló Pascual, 1947, reviews briefly the history of the treatment of pulmonary tuberculosis previous to the introduction of pneumothorax, and continues with sections on the macroscopic and histopathological anatomy of the collapsed lung, the mechanism of collapse and collapse therapy. Brief clinical histories are given in an appendix. The book is illustrated and contains a bibliography.

The PNA acknowledges that it has profited greatly from the experience of similar organizations in other countries. Its founders visited antituberculosis centres abroad, studied their organization and were grateful for the advice of their directors. Their hope is now that the work and publications of the PNA will be of use to colleagues in other countries and they invite visitors to come and see what has been accomplished in Spain and the work in progress there in the campaign against tuberculosis. When present plans are completed, 20,000 beds will be available for tubercular patients and Spain will have one tuberculosis dispensary for every 100,000 citizens.

V. E. C. M.

[1] [For particulars see *Book Reviews*.]

1215

THIRD INTERAMERICAN CONGRESS OF SURGERY

We have received three volumes[1] containing the texts of papers and addresses read at the Third Interamerican Congress of Surgery held in Montevideo in October 1946. The congress was organized by the *Asociación de congresos interamericanos de cirugía*, whose function it is to arrange surgical congresses at two-yearly intervals, to which affiliated societies may send delegates. Usually, three special subjects are chosen for the attention of the congress, and on this occasion these were: Complications and sequelae of surgery of the biliary tracts, Surgical treatment of cancer of the oesophagus, and The treatment of fractures of the pelvis. The texts of papers on these and on other subjects are included in these volumes. Bibliographies, indexes and a list of the statutes of the Association, make up a very complete and interesting account of the congress.

V. E. C. M.

[1] [For particulars see *Book Reviews*.]

1216

THREE IMPORTANT NEW BRITISH JOURNALS

Was it in a flash of prophetic wisdom that the Preacher cried out that of the making of many books there is no end? But how else should it be? As the field of knowledge and enquiry grows ever wider it becomes inevitable that it must be divided and subdivided; and natural that each subdivision, as it amasses new facts, should demand a vehicle for the publication and dissemination of its findings and techniques. Three subdivisions which in the last year have found it necessary to seek their own medium of expression are social medicine, nutrition, and plastic surgery. Of these the last-named is by far the youngest and most highly specialized, while the first to some extent includes the broader aspects of the second.

British Journal of Social Medicine. In turning first to social medicine, it may not be inappropriate to recall that just a hundred years ago, in a revolutionary Europe, the conception of medicine as a social science was taking shape. In Britain, Chadwick's classic Report on the sanitary condition of the labouring population had been published and created no small stir; in 1848 the first Public Health Act was passed. Now at last social medicine has its own journal; no. 1, vol. 1 appeared in January, 1947, and the first volume of four parts has been successfully completed. It is one of the group of attractively-produced journals published by the British Medical Association, and is edited by Professors F. A. E. Crew and Lancelot Hogben with the assistance of a distinguished editorial committee.

The editors have defined the scope of social medicine in the following terms:

> As understood by those who are responsible for this Journal, social medicine is that branch of science which is concerned with: (*a*) biological needs, interactions, disabilities, and potentialities of human beings living in social aggregates; (*b*) numerical, structural, and functional changes of human populations in their biological and medical aspects . . . Social medicine takes within its province the study of all environmental agencies, living and non-living, relevant to health and efficiency, also fertility and population genetics, norms and ranges of variation with respect to individual differences and, finally, investigations directed to the assessment of a regimen of positive health.

It will be seen then that the field is, in one respect, a wide one, making possible the inclusion of a great diversity of papers, but these will be confined for the most part to "work done", and it is expressly stated that the journal "is not meant to provide a platform for those who wish to present their views concerning the place of social medicine in the organizational set-up of medicine as a whole." The full contents of this interesting new journal are given in the Guide to the Journals in the present and previous numbers of this Bulletin and may be seen to range from "Dietaries in maternity hospitals" to "Studies on age and wastage in industrial populations", or "School medical inspections, their value and limitations."

The size of the journal is convenient and the format very pleasing; one small but useful point which we noted with pleasure was that at the top of each article is given its correct bibliographical reference.

British Journal of Nutrition. While, as has been seen, some of the wider problems of nutrition fall within the sphere of social medicine, others come in the purely medical or biochemical fields. But in practice, articles on one or another aspect of nutrition have been scattered in a wide variety of journals. In the attempt to cover most of the field the editors of *Nutrition Abstracts and Reviews*, for example, are obliged to scrutinize several hundreds of periodicals from the world literature of which not more than perhaps half a dozen are devoted solely or mainly to nutrition.

Nutrition in Britain as a science *per se*, then, has long felt the need for having its own journal and now, with the appearance of the *British Journal of Nutrition*, this gap has, in part at least, been filled. The first number of vol. 1 appeared in September, 1947, and the volume has recently been completed by the appearance of a double number (2–3). It is the intention, however, that future volumes should consist of four quarterly parts. The journal is published by the Cambridge University Press for the Nutrition Society of Great Britain, and is edited by an editorial board, composed of names all well known in the nutrition world, under the chairmanship of Dr. S. K. Kon of the National Institute for Research in Dairying.

The first part of each number consists of original articles. These have dealt with e.g.: vitamin studies, the composition and nutritive value of certain foodstuffs, the food requirements of various domestic animals, haemoglobin levels in pregnant

women, and metabolic studies in starvation and severe undernutrition. The second part of the number contains the Proceedings of the Nutrition Society (both of the english and scottish groups), formerly published separately but now incorporated in the journal. The subjects of the three conferences of the Society reported in this volume are of more than sectional interest, dealing as they do with "Education in nutrition"; the "Preservation, colouring and flavouring of foods"; and "British needs and resources of calories, protein and calcium." In addition short abstracts of papers communicated to ordinary scientific meetings of the Society are given. The journal is well produced and printed and we look forward to future issues with interest.

British Journal of Plastic Surgery. It is little more than a year since the formation of the British Association of Plastic Surgeons; now they have celebrated their first birthday by the production of a very handsome first number of the British Journal of Plastic Surgery, the official organ of the Association. Though a comparatively young branch of surgery, plastic surgery received a powerful impetus through the demands made on it by the crippling and disfiguring injuries sustained in two world wars and it has made rapid and daring progress, sometimes with strikingly dramatic results. But it is not only to the injuries of war that plastic surgery has brought relief and rehabilitation; the art has been applied to the often equally disabling consequences of industrial accident, of burns, and of congenital defects.

In this first number the opening article, by Sir Harold Gillies and Dr. R. J. Harrison, treats of a rare condition, congenital absence of the penis, and of the details of operative reconstruction —phalloplasty. The next article, of wider appeal, by Sir Archibald McIndoe, deals with deformities of the male urethra. In the third article, Mr. Rainsford Mowlem describes an operation involving the construction of a "lymphatic bridge" in the treatment of lymphoedema. Two articles, by Mr. J. B. Cuthbert and Mr. F. T. Moore, respectively, deal with the pollicization of the index finger after loss of the thumb; while in the last article Mr. M. C. Oldfield describes an operation for repair in the congenital condition of syndactyly.

The journal, which will not be confined to the field of a specialty but will include contributions from all allied branches of surgery and dentistry, has been launched with the blessings of the President of the Royal College of Surgeons of England and of a past President of the Royal College of Surgeons of Edinburgh. Professor Paterson Ross contributes a very interesting note on postgraduate surgical training, in which he discusses the relationship of the specialist surgeon to the general surgeon, and of the specialists to each other, and shows how they may derive mutual benefit.

The editor, Mr. A. B. Wallace of the Department of Surgery, Edinburgh University, and the publishers, Messrs. E. & S. Livingstone, are to be congratulated on this very fine production.

To these three new journals we venture to offer a welcome and to wish them a long and fruitful life. For surely Ecclesiastes was altogether too gloomy in thinking that much wisdom is much grief and he that increaseth knowledge increaseth sorrow.

1217

BULLETIN OF THE WORLD HEALTH ORGANIZATION

We have received the first number of this long-awaited periodical, which replaces not only the *Bulletin of the Health Organisation* of the League of Nations but also the *Bulletin mensuel de l'Office international d'Hygiène publique*. For the present it is being published in only two editions, english and french, but it is hoped later to publish it in several other languages. It will contain communications submitted by representatives of the Member States during the sessions of the Assembly and of the Executive Council, official reports from the expert committees, and original articles by experts and specialists attached to WHO. As pointed out in the editorial, however, the new health organization has a wider scope than its forerunners and this may be expected to influence the final character of the *Bulletin*. This first number, in the nature of its contents as well as in format and general lay-out, closely resembles the old League of Nations publication. Nearly half the space is taken up by an article on tuberculosis in Greece illustrated by well-reproduced photographs. For the rest, there are reports from two expert committees, on biological standardization and on malaria; a series of notes on the immunity reaction after vaccination and on post-vaccinal encephalitis (two of the urgent questions referred to the Interim Commission of the new organization by the Office international d'Hygiène publique); and articles on rodent infestation in ships, on relapsing fever, and on the anti-malaria campaign in Greece in 1946. The periodical is well printed on reasonably good-quality paper and shows evidence of careful editing. Bibliographical references, for instance, are uniform in style for the most part, the abbreviations of the titles of periodicals being appropriately enough, in accordance with the code drawn up by the International Institute of Intellectual Co-operation in 1930, a style now familar to english readers through its use in the *World List of Scientific Periodicals* and in a large number of scientific periodicals published in this country and in America. There are however a few cases as, e.g. on p. 197, where authorities are quoted in the text without any reference being given, a practice that causes much annoyance and loss of time to anyone wishing to consult the originals. We wish the new Bulletin well and heartily share the editor's hope that it may become a medium for forging strong intellectual links between its readers in all countries.

Cyril C. Barnard

1218

SURGICAL ANNALS

The *Annals of the Royal College of Surgeons of England*, which began publication in July 1947, has now completed its first volume. As explained by Sir Alfred Webb-Johnson, the President, in a Foreword, the new journal is designed to serve as a medium for the publication of lectures delivered at the College and will also include items of historical interest, accounts of recent events, and a diary of forthcoming functions, lectures and practical classes. The decision of the College to make the world conversant with recent advances in surgery and with the corporation's multifarious activities by the publication of its own journal will be widely welcomed. The journal is issued monthly and is edited by Sir Cecil Wakeley; format and general production are excellent. In the past the medical corporations of Great Britain have been responsible for the publication of many books, catalogues and reports, but, unlike the Colleges of Physicians and Surgeons of America, they have never issued their own journals over any considerable period. We cannot remember any british journal comparable in scope and purpose to the *Annals*, but honourable mention must be made of the *Medical Transactions* published by the Royal College of Physicians, in six volumes, between 1768 and 1820.

The first volume of the new journal contains lectures by Major-General Philip Mitchiner on gangrene and on surgery in two wars; by A. C. Lendrum on painful tumours of the skin; by R. W. Nevin on the surgical aspects of intestinal amoebiasis; by H. S. Souttar on recent advances in the treatment of carcinoma of the oesophagus; by V. E. Negus on injuries and cicatricial stenosis of the larynx; by Sir Lionel Whitby on blood transfusion and intravenous therapy; by Rainsford Mowlem on the replacement of skin losses in traumatic injuries; by E. Sprawson on foods and feeding as they affect teeth and their environment; by W. K. Livingston on physiological responses to wounding; by R. J. V. Pulvertaft on post-operative pulmonary embolism; by T. Cecil Gray on the use of d-tubocurarine chloride in anaesthesia; by M. Forrester-Brown on operative procedures in poliomyelitis; by J. R. Learmonth on the problems of portal hypertension; and by Sir Cecil Wakeley on vogue and fashion in abdominal surgery. There are contributions by three of the most distinguished american surgeons of the present day: Dr. Frank Lahey's Cecil Joll Lecture on hyperthyroidism; Dr. Arthur W. Allen's Moynihan Lecture on duodenal ulcer; and Dr. Evarts Graham's Lister Oration on some aspects of bronchiogenic carcinoma. Several articles and notes deal with the Royal College itself. Professor Willis writes on the Museum of Pathology and Mr. Le Fanu on the vicissitudes of the College Library during the war. On the historical side we note the Vicary Lectures of Sir Arthur MacNalty on the Renaissance and its influence on english medicine, surgery and public health and of Dr. E. Ashworth Underwood on naval medicine in the reigns of Elizabeth and James the First. Sir Arthur Keith breaks new ground in writing on John Hunter as a psychologist and Sir Heneage Ogilvie writes on a hundred years of gastric surgery. Interesting notes on

Hunter's bust in Leicester Square and on "Robin Adair," the romantic eighteenth century surgeon, appear over the initials of the distinguished President of the College.

W. J. B.

1219

MEDICAL BOOKMAN AND HISTORIAN

The Medical Bookman and Historian, a monthly journal now in its second volume, commenced publication in January 1947, as the *Medical Bookman*. By November it had established itself and, under the direction of a distinguished editorial board, was renamed *The Medical Bookman and Historian*. In this form it represents the first english journal devoted to the cultural and historical aspects of medicine.

1220

EXCERPTA MEDICA

This is a dutch enterprise with its central administration in Amsterdam, and a chief Editorial Board of three, headed by Prof. M. W. Woerdeman to direct the general medical side of the project. Vol. 1, no. 1 of most sections appeared in 1947 and a few are still awaited in 1948.

Excerpta Medica aims at providing a comprehensive abstracting service of world medical literature to replace such reliable journals as the *Zentralblätter* and *Berichte* of Julius Springer Verlag, Berlin, that have totally disappeared during the war years. Its service is claimed to be more comprehensive and wide-spread than any provided by earlier journals, and it is proposed to include abstracts of every article published in every available medical journal in the world. They will all appear in the english language and will be arranged in separate sectional journals as follows: Section I Anatomy, Anthropology, Embryology and Histology; Section II Physiology, Biochemistry and Pharmacology; Section III Endocrinology; Section IV Public Health and Social and Industrial Medicine; Section V General Pathology, Pathological Anatomy and Bacteriology; Section VI Internal Medicine; Section VII Pediatrics; Section VIII Neurology and Psychiatry; Section IX Surgery; Section X Obstetrics and Gynaecology; Section XI Oto-, Rhino-, Laryngology; Section XII Ophthalmology; Section XIII Dermatology and Venereology; Section XIV Radiology; Section XV Tuberculosis.

1221

A NEW SPANISH ABSTRACTING AND INFORMATION SERVICE

Boletín Noticiario Internacional Médico (Madrid) is a new weekly journal designed to provide medical men in Spain with abstracts in Spanish of important articles originally published in other countries, especially the USA, Great Britain, France, Switzerland, Sweden, Italy and the Argentine. The editors undertake to obtain for readers a reprint of any complete article in its original language or in Spanish, and it is hoped to form a library containing works by specialists in Spain and elsewhere. It is hoped also to have a translation service, in connexion with the library, which would specialize in medical translations. Films from the USA will be shown from time to time. The first number (vol. 1, no. 1, February 1947) of this journal contains abstracts from various british and american journals.

1222

A NEW MICROFILM SERVICE

In the first number of *Unesco Monitor* (August 1947, published from Unesco House, Paris), which contains mainly information about educational and cultural activities, the following note is inserted:—

A new microfilm service to spread knowledge on bacteriology and allied sciences has been put into operation by the Pasteur Institute of France.

The service is free of charge to all who require literature on research methods in bacteriology. Upon request, the Pasteur Institute will supply microfilms of any article in the reviews and journals available.

It is expected that the service will greatly assist the dissemination of information on the latest materials and techniques in that field of science.

1223

AN ASSOCIATION OF MEDICAL LIBRARIANS

The need for an association of medical librarians which would correspond, for instance, to the Medical Library Association of America, has long been felt in Great Britain, the formation of such a body having actually been suggested by Sir William Osler, as long ago as 1909, at the annual meeting of the British Medical Association. This need has now been met by the formation of a medical subsection of the Library Association, under the chairmanship of Mr. C. C. Barnard, Librarian of the London School of Hygiene and Tropical Medicine; the inaugural meeting was held on 4 October 1947 and attended by librarians from medical institutions in all parts of the country. Membership is confined to members of the Library Association, but medical men and others interested will always be welcomed as guests at meetings.

The principal projects designed to increase the efficiency of the medical library service consist of: the compilation of a union list of medical periodicals, which will serve as a guide to the sets held in british libraries; inter-library loans; and an exchange system for duplicate and unwanted books and periodicals, which will help librarians to complete imperfect sets. A monthly bulletin is also being issued, both as a medium for the exchange of news and views and as a link between members separated by distance and unable to attend all the meetings.

In addition to these activities, regular meetings will be held, at which talks by medical men and others will be given, and papers on technical and bibliographical questions will be read and discussed; visits to places of professional interest will also be made.

The first meeting of this kind was held at the National Institute for Medical Research, Hampstead, and was well attended, both by librarians and the medical profession. The subsection was welcomed to the Institute by the Director, Dr. C. R. Harington, and the meeting was then addressed by Dr. George Popják, of the Biophysics Department of the Institute, who gave a very interesting talk on Elementary Biophysics; finally, Miss Wigmore, the librarian, outlined the history of the library and members and guests were shown its many interesting features. The success of this meeting, which owed much to the kind co-operation of the National Institute for Medical Research, augurs well for the future.

The secretary of the subsection, Mr. W. J. Bishop, of the Wellcome Historical Medical Library, 183 Euston Road, London, N.W.1, will gladly answer enquiries from librarians and members of the medical profession.

H. M. C.
A. H.-S.

1224

PUBLICATIONS AND REPORTS

From Argentina comes an interesting report of work done there for sufferers from leprosy and for their dependants. This report, entitled *Memoria correspondiente al ejercicio vencido el 30 de abril de 1944*, is published by the Patronato de Leprosos of Argentina and contains a comprehensive account of the work done during that year by the various committees and societies affiliated to the Patronato. Reports from the regional leper centres throughout the country are included, as well as a list of donations received, and an index. The report is illustrated with photographs of colonies under the control of the Patronato de Leprosos, and of the preventive colonies where children of leper parents are cared for.

The Instituto de Perfeccionamiento Médico-Quirúrgico, Buenos Aires, has sent us a copy of *Conferencias—1945*. This book contains the text of a number of lectures delivered during that year. The subjects dealt with include total gastrectomy in cancer

of the stomach (Professor I. Goni Moreno), conservative treatment for gangrene of the extremities (L. Feldman), observations on the clinical, radiological and surgical interpretation of disorders of dental origin of interest to the surgeon (R. A. Vivone), and a general review of homoeopathic treatment as applicable to surgical cases (A. N. Mazetti). The book is illustrated with photographs, tables and diagrams and an index is included.

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The Institut de Recherches sur le Cancer de Lille was founded in 1936 by a franco-american effort of co-operation, and is the only establishment in France devoted exclusively to research, as opposed to the clinical problems of diagnosis and treatment, on the subject of cancer.

We have received a report (*Institut de recherches sur le cancer de Lille*, Cité Hospitalière, Lille, 1946) issued by this institution, which describes its foundation, objects, general organization and methods of work in some detail. The work carried out at the Institute since its opening in 1939 is summarized in two sections: the annual reports of the director, and a bibliography of papers published by members of the staff. A section of photographs of the building and details of the administrative council and technical staff are also given.

JOURNALS NEWLY RECEIVED

Notes on journals received for the first time, usually in exchange with the British Medical Bulletin

Jornada Médica (Buenos Aires) is a new journal, of which vol. 1, no. 1 appeared in June 1947. It is published monthly and is designed principally for medical practitioners whose time for reading is limited but who wish to keep abreast of new developments in medicine. Both theoretical and clinical aspects of medicine will receive attention and the editors hope their journal will help to disseminate knowledge and thereby prove beneficial to patients. The first number contains four original articles, dealing with the clinical aspect and treatment of amoebiasis by Dr. Silvio Parodi, the construction and grafting of a finger by Dr. Francisco E. Arespacochaga, influenza and seasonal colds by Drs. Hernán Gonzalez and Carlos Floriani, and acute intestinal obstruction by Dr. Armando F. Giordano. A special section is devoted to translated extracts from the *Archives of Internal Medicine* and further sections contain abstracts from other journals and bibliographical comments.

The *Boletín Mensual* of the *Instituto Nacional de Previsión Social* (Buenos Aires) is a monthly journal which began publication in 1946. In the editorial of vol. 1, no. 1 (October 1946), the first number we received, the hope is expressed that this new journal will play a useful part in the investigation of social problems in Argentina, in finding a solution for them, and in awakening the public conscience to their existence. The Instituto Nacional carries out investigations and research into social questions and in this number of its journal publishes some of the results of its enquiries. The first article is contributed by members of the legal department of the Institute and examines the legal position of illegitimate children in Argentina. The text of resolutions and decrees made by the Institute is also included, with statistics relating to its finances.

The *Revista Médica de Rosario*, of which year 37, nos. 5 and 6, May and June 1947 have been received, is the official organ of the Círculo Médico de Rosario, Argentina. The May number contains four original articles and book-review and abstract sections. The June number contains six original articles, book-review and abstract sections and notes of meetings of medical societies in Rosario.

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From Australia come the *Clinical Reports of the Adelaide Children's Hospital*, vol. 1, no. 1, May 1947, the first attempt to publish details of the work of this hospital, at which, in 1947, 5,557 children were treated as in-patients, and 65,072 as out-patients. The *Clinical Reports* are to appear from time to time and the Editorial Committee plans to publish the second number in November 1947. While the Committee realizes that papers in the journal must generally be based on continued medical practice, it hopes that they may contribute to the sum total of knowledge and to the wellbeing of the child. There are articles in this number on The treatment of influenzal meningitis, Leukaemia in children, and Acute osteomyelitis treated by penicillin. *Clinical Reports* should be a useful addition to the small number of paediatric journals in the english language.

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The first number of vol. 2 (January 1947) of *Klinische Medizin* was received from Vienna. This journal, sub-titled "austrian journal for scientific and clinical medicine", appears on the 1 and 15 of each month and is published by Urban & Schwarzenberg. The price per quarter is S.18, per single number S.4. All editorial communications should be directed to Prof. Dr. L. Arzt, Wien IX, Alserstrasse 4.

Among the original articles in this number are communications on the mechanism of aerophagy, infectious diseases in Austria in 1946, diagnosis and therapy of typhus, and the radiography of joints. A section of abstracts of articles in other journals is also included—in this number all from the *British Medical Journal*.

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Copies of two publications issued by the University of Minas Gerais have reached us. The first of these is the *Anais da Faculdade de Medicina* of the University (year 4, vol. 2, 1945), which consist of the texts of four lectures delivered by members of the Faculty of Medicine and six original articles. These lectures and articles deal with diverse subjects, which include a study of changes in the blood serum in 100 cases of leprosy (O. Versiani Caldeira & E. A. de Cerqueira), clinical notes of a patient suffering from cobra-bite (O. de Magalhães), and a study of the prophylactic and therapeutic properties of sulphadiazine, sulphapyridine and sulphanilamide, especially in malaria (S. Americano Freire, C. Cristoff & W. Lobato Paraense).

The second of the publications is the *Anuario da Faculdade de Medicina* (year 5, vol. 3, 1946). This journal is composed of reprints of ten articles contributed to brazilian journals by members of the Faculty.

Anais da Faculdade de Medicina do Recife. This journal is the official organ of the faculty of medicine of Recife, Brazil, and no. 10–11 for years 10 and 11 (1943–1944), published in 1946, has been received. This number contains three articles, the first being a contribution to the study of yaws (J. Lôbo). The second article, on Manson's schistosomiasis, is the text of a lecture delivered at a medical congress in Recife by Dr. H. Menezes, and the third article deals with cutaneous amoebiasis (S. Campos). This number also contains a book-review section and statistics issued by the department of morbid anatomy.

Arquivos de Clinica (Rio de Janeiro) is now in its third year of publication and no. 3 of vol. 3 for September 1946 has been received. This number contains the second part of an article, the first part of which appeared in the previous number, on clinical haematology (Michel Jamra), an account of inflammatory lesions of granulomatous type seen in human visceral leishmaniasis (Luigi Boglioli) and a contribution on the treatment of liver disease (S. A. Portis). An account of some meetings of the Faculty of Medicine of Rio de Janeiro and news and abstract sections complete the contents.

Arquivos da Faculdade Nacional de Medicina is the official organ of the faculty of medicine of Brazil University and is published in Rio de Janeiro. It was founded in 1946, the first number being dated July 1946. The journal publishes original articles, and this number contains nine contributions which include the following: sclerosing bone sarcoma of the femur with clinical notes (Castro Araujo), the metabolism of iodine (A. Couceiro & E. De Robertis, and oligophrenia accompanied by multiple intercranial calcifications (J. L. Lopes).

Brasil Médico-Cirúrgico (Rio de Janeiro) year 8, no. 5–6, October-December 1946, contains four original articles dealing respectively with pulmonary embolism, by Drs. Egidio S. Mazzei, Taylor Gorostiaga & Elyeser Magalhães; sigmoiditis with

perforation, by Drs. Adolfo Dujovich & S. Form; gastro-enterology, by Dr. Manoel F. Garcia; and the historical foundations for specialization in the field of internal medicine, by Dr. Pedro Nava. The section of notes for practitioners, which is a regular feature of this journal, gives in this number clinical details of some cases of diphtheria in children. In conclusion there is a list of journals received, and a news section.

Also from Brazil comes *Ginecologia* (Recife), which appears every two months, and which started publication in 1946. We have received no. 4 (August 1946), which contains three original articles, including a contribution from Dr. James Young dealing with the development of obstetrical studies in Great Britain, and some notes on medical folklore among primitive peoples by Dr. Ferreyra dos Santos. The journal also gives detailed accounts of the opening ceremonies of the new Universities of Bahia and Recife.

Neuronio is a quarterly bibliographical journal published in São Paulo, of which we have received vol. 8, no. 1, for the first quarter of 1947. This journal publishes in Portuguese abstracts from latin-american journals, and also from time to time original articles. The present number contains 26 pages chiefly devoted to abstracts arranged under subject headings, and there is a short news-section.

Revista de Higiene e Saúde Pública (Rio de Janeiro) is the official organ of the Sociedade Brasileira de Higiene. The number for April—June 1947 inaugurated a new series of the journal, then in its fifth year of publication. The editorial expresses the hope that the journal will play a useful part in the work for the betterment of world health. The number opens with a biographical note on Dr. Fred Lowe Soper, a member of the Sociedade Brasileira de Higiene, recently appointed director of the Pan-American Health Division in Washington. Other features are articles on the importance and geographical distribution of some of the mosquitoes found in Brazil, and on the diseases prevalent in the province of Alagôas. News and abstract-sections are also included.

We have received for the first time a copy of *Revista Medica Municipal* (Rio de Janeiro) a periodical which is published quarterly and is the official organ of the Public Health authorities. This issue, no. 1 of vol. 8, contains five original articles, which include a contribution from Dr. Joaquim de Brito on the treatment of stomach wounds from various causes, a review by Dr. Leão de Aquino of some outstanding events in the history of the Hospital Sanitório São Sebastião, with the text of addresses and articles published at various times in connexion with these events, and an article by Dr. Herminio Linhares on meningo-encephalitis in rats caused by a filtrable virus. Sections containing news, book reviews, abstracts from foreign journals, lists of journals received and their contents complete the number.

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S'vremenna Pediatriya (Contemporary Pediatrics) (Sofia), year 1, vol. 1, no. 7–8, 1947 is largely devoted to full abstracts of papers in world medical journals, on paediatrics and related subjects. The first article is an abbreviated version in Bulgarian of a paper on scabies by Gordon & Unsworth (*Brit. med. Bull.* 1945, **3**, 209, *BMB* **776**).

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Archivos de la Sociedad de Cirujanos de Hospital (Santiago de Chile) is a quarterly journal for surgeons of which we have recently received no. 2 of vol. 16, which appeared in June 1946. This number is divided into four sections, the first of which contains fifteen original articles. Among these are articles dealing with emergency treatment for gastro-duodenal ulcer by Dr. Marcial Baeza, melorheostosis by Dr. Orlando Poblete Nuñez, anal fissure by Dr. A. Schwartz, and acute torsion of the great omentum by Dr. Adolfo Dujovich. Most of the articles contain clinical histories of patients treated by the authors, with details of the response to the treatment given. The second section gives particulars of lectures and conferences of special interest to readers of the *Archivos*, and the remaining sections contain abstracts, notices and news.

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Repertorio de Medicina y Cirugía (Bogotá) was founded in 1909 to assist in the dissemination of medical knowledge in Colombia. No. 5 of vol. 2, July 1947, contains five original articles (on rabies, cancer of the gravid uterus, two surgical conditions, and menstrual epilepsy) and the first of a series of lectures on anaesthesia. Summaries in Spanish, and in some cases a bibliography, are given at the end of each article.

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Among the journals from Czechoslovakia reaching us for the first time is the *Bratislavské Lekárske Listy*, the journal of the Slovak University Medical Faculty and of the Slovak Medical Association, vol. 26, no. 9, September 1946. An effort is made to obviate the barrier raised by the use of the slovak language by giving lengthy summaries in Russian, English, French and German. In the english summaries, the translation is very literal, the spelling is sometimes phonetic, and there are many printer's errors; however, through these obscurities the general meaning of the articles appears, and the purpose of the summaries is achieved.

There are original articles on: complications of wounds of the cranium, Raynaud's disease, myocardial infarction in youth, surgical therapy and roentgenotherapy of struma, treatment of lip cancer.

We have also received vol. 47, no. 8 (1947) of *Ceskoslovenska Stomatologie*. Although it is an attractively produced journal on good paper, printed in clear type, it does not look for readers outside Czechoslovakia, as no summaries are given in other languages to guide the western european reader to its contents. What is more useful from the czech standpoint is the inclusion of comprehensive abstracts from world literature on dental subjects.

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Anales (Quito) is the official organ of the Universidad Central de Ecuador, which was founded in 1651. No. 322 of vol. 73 (January—December 1945) contains some very interesting features. There are sections dealing with medicine, history, education and literature. The medical section contains the text of a lecture on cancerology delivered by Dr. César Ricardo Descalzi at the Hospital Civil de San Juan de Dios, and a detailed study of three cases of erythroblastosis by Professor César Jacome. Professor Gonzalo Rubio Orbe contributes an interesting study of the Ecuador Indians, and also included in this number are some chapters of a work on the history of Ecuador in ancient and modern times which are being published in serial form, by Dr. C. Reginald Enock, F.R.G.S. The section of University news gives a summary of the chief events of the academic year 1945–46.

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Le Progrès Médical (Paris) is a well-known weekly of high standing, now provisionally appearing twice monthly, under the editorship of Professor Maurice Loeper and Dr. Maurice Genty. Apart from original articles and reports of lectures, it contains brief accounts of society meetings, abstracts of articles from both french and foreign journals, a section on the history of medicine, and a notes-and-news section. The subjects of the original articles in the number for 24 June 1947 (year 75, no. 12) are: Neptal and hypertonic subtosan (M. Perrault & P. Rousseau); Incomplete physiological section of the spinal cord (J.-A. Chavany); and An attempt to find a biochemical test of the activity of massive rectal doses of vitamin D_2 (J. Desbordes & G. Feuillet). A report of a lecture by J. Boureau on Analgesia and anaesthesia in obstetrics is also given, and a further interesting feature is an article by G. Barraud, in the historical section, on roman medicine.

Le Journal de Physique et le Radium (Paris), of which we have received the number for February 1947 (series 8, vol. 8, no. 2), is published by the Société française de Physique. The main part of the journal is devoted to original articles, of obviously high scientific standard, on subjects connected with physics and radium; the majority of these are preceded by brief summaries. There is also a section of abstracts of articles from french and foreign chemical and physical journals, arranged under subject-headings; and finally a section containing reports of meetings of the Société française de Physique. The two last-named sections each have their own pagination followed by appropriate symbols. The typographical format is clear and of a standard

worthy of the subject-matter of the journal, while it is noteworthy that importance is obviously given to matters of style in such items as bibliographies and headings of abstracts.

Another french journal which we have received is *Monde et Médecine* (Paris), edited by J.-R. Frugier, with the assistance of a distinguished editorial committee, and published by Les Editions Universelles. Its sub-title describes it as an international review of the medical sciences, and the two numbers we have seen (no. 10, October—November 1946, and no. 11, December 1946—January 1947) consist entirely of original articles, mostly clinical, though some are of a more general nature, such as a report on the commemoration of the fiftieth anniversary of Pasteur's death, and an article on the effects of the atomic explosion at Hiroshima.

La Revue Générale de Médecine et de Chirurgie de l'Union Française (Algiers), now appearing once a month instead of three times a month as in pre-war days, is issued by the Société d'Expansion Médicale et Pharmaceutique. It publishes review articles, sometimes original, sometimes reproduced from french or foreign journals, on subjects of particular interest to the general practitioner in the french colonies. It also includes a bibliography section. The number for March 1947 (year 24, no. 494) consists of 14 articles, all reproduced from french journals, and the bibliography section, containing reviews of some half-dozen books.

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After six years of interruption, due to enemy occupation and postwar difficulties, we welcome the re-appearance from Athens of the *Archives of Hygiene* (third period, 5th year, January—March 1947, nos. 1–3). The journal is an impressive royal quarto production, printed in clear type on beautifully crisp paper, and well illustrated with large charts. Conditions of health in Greece during the war, the enemy occupation and postwar years are reviewed by the Director-General of Hygiene; there is a synopsis of epidemics in Europe, an account of the achievements of UNRRA as an international health organization, and of the creation of the World Health Organization to which Greece looks with other nations for aid, in the rehabilitation of the people's health. "On the occasion of the re-edition of the Archives of Hygiene" the editor states the journal's aim is "to give an historic and real picture" of the task of rehabilitation of the greek people and to put greek scientists in contact with the new methods and inventions of the war years so that they may be properly introduced into Greece.

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One of the most attractive of the new journals to reach us from Europe is the monthly international journal of paediatrics, *Paediatria Danubiana*, published in Budapest. Articles are published in English, Hungarian, Russian, French or German, together with summaries in all five languages. The journal is well printed and illustrated, and its pocket-size (20 × 15 cm.) convenient to handle.

In the foreword to the first number, the editor-in-chief, Professor P. Kiss, states the aim of the journal to be the endeavour "to broadcast the results of the research of doctors throughout the world who are striving to improve the health and happiness of children." The names of a large number (40 in vol. 2, no. 6) of editors from all over the world appear on the title-page.

The first number, which appeared in January, 1947, contained articles on renal diabetes accompanied by rickets, by R. Debré, Paris; on primary atelectasis and birth trauma, by A. Eckstein, Ankara; on a method for the radiographical diagnosis of ear diseases in infants, by C. Gefferth, Budapest; on the effect of penicillin after antrotomy in infants and children, by E. György, Budapest. In each number is a short section containing abstracts of articles on paediatrics, from journals of various countries; for example, in the first number, from the *British Medical Journal* and from the *British Medical Bulletin*.

Manuscripts and correspondence should be sent to the Editor, Bókay János-utca 53, Budapest VIII, Hungary. The annual subscription is 22 hungarian florins, or $9.

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We have received vol. 1, no. 1 of the *Indian Journal of Malariology*, March 1947. Since papers published in this excellent journal may be contributed from sources other than the Malaria Institute, this more general title has been chosen to replace the earlier *Journal of the Malaria Institute of India*. The latter had in 1938 succeeded the *Records of the Malaria Survey of India*. In vol. 1, no. 1 of the *Journal of the Malaria Institute of India*, the Director, Major-General Sir Gordon Covell, gave the history of the activities of the Malaria Survey of India from 1927–37. In the first number of its successor, he gives an account of the valuable work of the Malaria Institute of India from 1938–47.

Most of the contributions to this number are on malaria control, the de-weeding of tanks and ponds, the uses of insecticides with special reference to DDT; there is one clinical paper on certain aspects of paludrine.

Most interesting and useful bibliographical features are (a) the list of contents, arranged by volume and number, of the *Records of the Malaria Survey of India* and the *Journal of the Malaria Institute of India*, and (b) a classified list of publications from the beginning of the Malaria Survey of India in 1927, which forms Appendix III to the history of the Malaria Institute of India.

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Rassegna di Neuropsichiatria is the official organ of the Ospedale Psichiatrico Consortile di Nocera Inferiore, Salerno. This hospital was founded in 1883 and two years later began publication of a journal called *Il Manicomio* which was later replaced by *Archivio Generale di Neurologia, Psichiatria e Psicoanalisi*. The latter ceased publication during the war years and the *Rassegna di Neuropsichiatria* now takes its place. We have received for review vol. 1, nos. 1–2 of this new journal. The first article is by Professor Carmelo Ventra and gives an account of the Ospedale Psichiatrico during the years 1940–46. The area surrounding the hospital was heavily bombed and it suffered much damage, while problems of feeding and hygiene within the hospital became very difficult. The mortality rate began to rise in 1941, reaching its maximum in 1944, but since then has steadily declined. This number contains six further original articles, including one by Dr. L. Bini, of the Clinica delle Malattie Nervose e Mentali of Rome University, on the use of shock therapy in some unusual cases of psychosis. Clinical histories of cases treated are given. Dr. Domenico Rossi contributes an article on the psychopathology of chorea minor, and Dr. Giannetto Cerquetelli gives an account of his results in the treatment of multiple sclerosis with histamine. The journal also contains book review and news sections.

Annali d'Igiene is a journal published at two-monthly intervals under the auspices of the Istituto d'Igiene of Rome University. The first number to reach us is no. 1, of the 57th year, January—February 1947, which contains five main contributions. These include articles on exanthematous typhus during the italian expeditionary force's campaign in Russia (A. Spezzaferri), some enzymatic properties of penicillin (F. Mulè) and an investigation into the question of whether an ultravirus may cause whooping cough (M. Carpano). This number also contains abstract and news sections.

Another journal from Rome is the *Giornale di Medicina Militare*, published under the auspices of the Direzione Generale di Sanità Militare, and now in its 94th year of publication. No. 5 for September—October 1947 contains articles on physical work and emotion in the pathogenesis of "soldier's heart" (G. Donati), peritonitis following perforation of the small intestine in typhoid (E. Zaffiro), and an account of gangrenous lung abscess with empyema cured by penicillin (P. Scaduto & A. Cimino). Also included are abstract and news sections.

Published in Naples, *Archivio di Tisiologia* appears at two-monthly intervals, and no. 4 of vol. 2, 1947 contains approximately 172 pages. The journal is divided into two distinct sections with separate paginations, the first being devoted to topics of general medical interest, and the second containing main articles on tuberculosis and allied subjects. The former section in this number contains accounts of three congresses held in Britain on tuberculosis and public health. The first of these articles, which is accompanied by an english translation, is an account of the Edinburgh Congress of 16–19 July 1947, to which the author was invited. He records his impressions of the Congress, and also of his subsequent visits to sanatoria and health centres in Britain. British clinical methods and operative techniques are compared with italian procedure.

Tumori (Milan), the official organ of the Istituto Nazionale per lo Studio e la Cura dei Tumori, is published at two-monthly intervals and is now in its 34th year. We have received no. 1–2 of vol. 21, series 2 1947, which contains eight original contributions. The first article of this number reviews the activities of the Institute since its foundation in 1928. Mention is made of much-appreciated gifts of books to the library from the USA, Britain and France, of the inauguration of a committee whose members visit the sick poor in their homes, and of the work of the various departments of the Institute. There are seven other original articles and an abstract section.

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Sugestiones (Mexico) contains some interesting features. In the number for June 1947 (year 11, no. 142) is a transcription of some pages from the book by Professor Alejandro A. Bogomolets on the prolongation of life. This particular passage discusses the question of what might be considered a normal life-span and gives a number of instances of continued human activity to an advanced age. An article on leprosy in Monterrey is contributed by Dr. A. Peyri who was formerly in charge of the leper island of Providencia. He gives details of treatments given to some of his patients and of the results obtained. Dr. J. López Durán writes on sex hormones, and there are also articles on the treatment of anaemia by Dr. J. G. Isabet, the use of vitamin D in the treatment of some skin diseases by Dr. José F. Brun, complete arrhythmia and mitral stenosis by Dr. Jorge Meneses Hoyos, a study by Dr. Pavón Serrelangue of a case of partial control of the autonomic nervous system, the diagnosis and treatment of deep wounds of the praecordium by Dr. Joaquín Maass Patiño, and the problem of malnutrition by Dr. Ramón Osurio y Carvajal. The journal also contains a section of bibliographical notes, a list of new books, and an article by Dr. Fausto Zerón Medina, in the *Artistas Médicos* section, on the doctor-poet Gabriel Guerrero Ibarra.

Also from Mexico comes *Química y Farmacia* (vol. 12, no. 109, January 1947). This journal is the official organ of the Colegio de Químico-Farmacéuticos Biológicos de México, and the number under review is the first to reach us. The editorial of this number emphasizes the need for co-operation between all peoples in order to further human progress. The contents include an article on the determination of the carotene, fat and protein content in maize; Part VI of a study of alchemy, medicine, pharmacy and pharmacopoeias from the 16th to the 20th centuries; biographical notes on Leopoldo Rio de la Loza, a chemist, and Andres del Rio, a mineralogist; and a study of popular nutrition in Mexico, which stresses the advisability of increasing the cultivation of maize.

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The *Boletín del Ateneo Médico de Lima* publishes original articles on medical subjects with clinical histories of interesting cases, and also has a section containing abstracts from journals published in Spanish. The first three numbers of this journal to reach us were: vol. 2, nos. 1, 2, 3 (January—June 1947).

Another peruvian journal is the *Boletín de la Sociedad Química del Peru* (Lima, vol. 12, no. 4, December 1947). This number contains articles and the first instalment of the memoirs of Fernando C. Fuchs Carrera. Señor Fuchs Carrera has been connected with mining in Peru for fifty years and his memoirs are to be continued in serial form in subsequent numbers. Notes of the Sociedad Química and a list of publications received are also included.

La Protección Materno-infantil en los Últimos Cinco Años, Lima, is a report for the years 1940–1944, published by the peruvian Ministry of Health on its work on behalf of mothers and children. During the period reviewed the number of prenatal clinics and dispensaries for mothers and children was increased, and home-nursing facilities improved. It is noted that during these years there has been an encouraging decrease in infant mortality. The report gives an account of the present organization of the maternity and child-welfare services in Peru, and there is an appendix summarizing the principal resolutions and decrees in operation for the protection of mothers and children.

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The first number of the fortnightly journal, *Nowiny Lekarskie Dwutygodnik Spoleczno-Naukowy*, to reach us from Poland is vol. 54, no. 21, 1947. The two main contributions are: a paper by Tomaszewski on vitamin A in health and disease, reviewing the subject and giving the results of his own research, as published in various polish journals and in the *Edinburgh Medical Journal*; and an account of two cases of polyradiculoneuritis by Jasiński. There are also items of polish medical news and a reproduction of the British Council Monthly Lists of new british medical publications for July and August 1947.

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Revista de Psicología General y Aplicada (Madrid) has been founded in order to form a link between all those who are interested in psychological problems, and as a medium for the exchange of information. The journal is published quarterly and each number will contain, in addition to original articles of psychological interest, information about new publications of interest to specialists in psychology. It has also been arranged to publish in each number a translation of an article from the *Psychological Review*, the organ of the American Psychological Association. From time to time an entire number will be devoted to some current psychological problem.

The first number (vol. 1, no. 1, 1946) of this journal contains 316 pages and six original articles, and also sections containing notes on laboratory tests and apparatus, bibliographical notes, reviews and news.

Archivos de Enfermedades del Corazón y Vasos (Barcelona) was founded in 1922 and is the organ of the Instituto de Medicina Práctica. The February—March number of vol. 30 (1947) contains three original articles, the first being a study of the arterial pulse and its dichrotic waves by Professor M. Bañuelos, of the Faculty of Medicine, Valladolid. Dr. Domingo de G. Durán Arrom contributes an article on certain diseases, such as rheumatism, arterial hypertension and cardiovascular syphilis, which damage the circulatory system. Dr. Arrom also contributes a section of clinical notes on cardiological practice. This number contains in addition a section of aphorisms, a therapeutic index, a news section containing abstracts from other journals and a bibliographical section.

Galicia-clínica (Corunna), is a monthly journal which publishes articles, news and book reviews of medical interest. No. 1, year 19, January 1947, contains 68 pages, and includes articles dealing with the treatment of burns (E. Sández Figueiras), the treatment of osteomyelitis (A. J. Echeverri), haemocultures and agglutination reactions and the interpretation of results (F. Beato), the extraction of foreign bodies from the oesophagus (Ortega). The news and book-review section gives information about appointments, events and new publications in Spain of medical interest.

Odontoiatría (Madrid) is described as an ibero-american journal devoted to the study of the mouth, its disorders and treatment. No. 23 of vol. 2, November 1945, the first to be received by us, contains four articles which include contributions on vitamin C in relation to gingivitis (J. S. Restarki & M. Pijoan), dental affections commonly found in air-crews (S. Forteza), and the psychological study of the patient (B. Martínez-Gil de Bretón). In addition, this number contains an editorial, book reviews printed on perforated pages to facilitate their easy removal for filing, and an abstract section.

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During 1947, we received vol. 21, nos. 1–3 of the *Quarterly Bulletin of Northwestern University Medical School* (Chicago). This beautifully-produced journal is printed in clear type on fine paper, and it has many good charts and illustrations. It is divided into two main sections, scientific and general; in addition there are an editorial, news of the Medical School, and a list of recent publications of the Medical School Faculty. Among the more interesting of the scientific papers are a series on work at high altitude, by Friedemann, Ivy and collaborators; and recent advances in hepatic and biliary disease, by Snell, with references to recent work.

The section General Contributions, includes historical and bibliographical studies, one, for example, by Laufmann on surgical haemostasis through the ages; and also papers recording the professional experiences of members of the Medical School in Italy and India.

The *Journal of the American Medical Women's Association* is another american journal linked to a medical institution, the New York Infirmary. This number (vol. 2, no. 3, 1947) has been contributed by the staff of the Infirmary; the scientific section includes articles on intra-uterine irradiation, the Rh factor in obstetrics, child guidance, a symposium on recent advances in therapy, and case reports.

The feature papers describe the history of the Infirmary, its traditions and present needs. It is well produced and documented, and includes a specially interesting feature in the list of current publications by women in medicine and in allied fields.

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The following journals have also been received:

Better Health (London), vol. **20**, no. 12, 1947
Boletín de la Asociación Odontológica Argentina (Buenos Aires), year **17**, no. 199, 1947
Bulletin of the Independent Biological Laboratories (Kefar-Malal, Palestine), vol. **5**, no. 3, 1947
Chinese Journal of Nutrition (Anshun, Kweichow), vol. **1**, no. 1, 1946
Héllinikiiatriki (Thessaloniki), year **17**, no. 1, 1948
Medisiinari Lääketieteenkandidaattiseuran Julkaisu (Helsinki) no. 3, 1947
Népegészségügy (Budapest), vol. **4**, no. 1–2, 1948
Oto-Nöro Oftalmoloji (Istanbul), vol. **1**, no. 1, 1946
Revista Ştiinţelor Medicale (Bucharest), vol. **37**, no. 1–2, 1948
Salud (Mexico D. F.), vol. **4**, no. 4, 1947
Türk Dişţabipleri Cemiyeti Mecmuasi (Istanbul), vol. **24**, no. 131–132–133, 1947
Výživa Lidu (Prague), vol. **2**, no. 11, 1947
Yaşamak Yolu Dergisi (Istanbul), no. 131–133, [1946]

* * *

1226

A MEDICAL PUBLISHER

Messrs. E. & S. Livingstone of Edinburgh, the well-known medical and scientific publishers, inform us that they have now opened a London office at 45 Lincoln's Inn Fields, London, W.C.2, where medical men desirous of inspecting the firm's publications are assured of a warm welcome.

Historical Notes

1227

PIERRE JANET (1859–1947)

The emergence of scientific psychology in the second half of the nineteenth century constituted a kind of intellectual epic. With this movement the name of Pierre Janet is indissolubly associated and due tribute is paid to this great french psychologist in *La Presse Médicale* for 23 August, 1947 (**55**, 561–562).

Pierre Janet was born in Paris on 30 May, 1859, and, after obtaining his " agrégation " in philosophy at the age of 23, taught for seven years at Le Havre. At the same time he worked at the municipal hospital where he was put in charge of a ward of neurotic cases; here he began his researches on hypnotism and the lower forms of mental activity, which formed the subject of his philosophy thesis, *L'automatisme psychologique*. This revolutionary attempt to apply hypnotism to psychology raised a storm on its presentation at the Sorbonne on 21 June, 1889. Soon after, he obtained a Paris appointment, and continued to lecture on philosophy while completing his studies in medicine and taking his doctor's degree. He then became head of the psychological laboratory at the Salpêtrière, where he worked first under Charcot and later under Raymond. In 1895 he began deputizing for Ribot as professor of experimental and comparative psychology and was officially appointed to the Chair in 1902. He occupied this position until 1934.

Janet's teaching was based on his minute observation of cases. He always took detailed notes of everything said by the patient and of every reaction, and classified his voluminous case-records like a botanical collection, habitually referring to them as his " herbier ". Most of his lectures were collected into book form and constitute the basis of his published works; some of the more important of these are: *L'état mental des hystériques* (1893), *Les obsessions et la psychasthénie* (1903), *Les médications psychologiques* (1919), *La médecine psychologique* (1923) and *De l'angoisse à l'extase* (1926–28). His teaching acquired a great reputation abroad, particularly in North America, where his influence was comparable only to that of Georges Dumas in South America.

The ruling idea throughout Janet's work—to establish a hierarchy of mental function based on *pathological psychology*—shows the influence of Ribot, with whom Janet came into contact early in his career. Ribot had been one of the first to apply scientific methods to psychology and, in particular, to obtain data valid for both disease and health from the analysis of mental disturbances, and it was this method which Janet adopted as the basis of his work. He maintained that there are two distinct forms of mental function: *automatic* or *conservative activity*, limited to reproducing the past, and *synthetic activity* which combines existing phenomena into new phenomena quite different from their component parts. The first activity is repetitive and the second creative. Normal thought is composed of both forms, but in weakened psychological conditions the synthetic activity gives way to the automatic.

Janet was a doctor as well as a psychologist. His name is linked with the syndrome of psychasthenia, which he was the first to differentiate and describe. His *La médecine psychologique* summarizes his experience as a psychotherapist. In this field he surpassed all his predecessors in the use of hypnosis and was at the same time one of the forerunners of the psychoanalysts. He made important observations on the cure of hysterical hypermnesia which led up to the psychoanalytic conception of " transforming the unconscious into the conscious ", but left it to Breuer and Freud actually to cross the threshold.

Janet found a source of satisfaction in his old age in following the rapid development of psychiatry; he lived to see many of his early ideas, which had been fiercely contested at the time, confirmed by modern methods of psychotherapy.

A. H.-S.

1228

WAYFARERS IN MEDICINE

The pathways of the medical pioneers, if not always smooth at the time of their first explorations, are easy and pleasant for those who follow by the comfortable process of imaginative reading. Our guide, on the occasion under review, is a well known Dublin surgeon, and editor of the *Irish Journal of Medical Science*, Mr. William Doolin. He is familiar with the ground, and the wayfarers are all old friends of his. Although each of the twenty-six essays is complete in itself, the book[1] preserves a chronological order, so that we pass from Imhotep to Sir Robert Jones, with such pleasant companions as Vesalius and Montaigne and Descartes and the less known Georges Mareschal, surgeon to Louis XIV. We accompany Ambroise Paré on some of his " Journeys in Divers Places ", we travel with Laënnec between Paris and his beloved Brittany, and we follow the career of General Gorgas who, by his war on yellow fever, made it possible for engineers to complete the Panama Canal and thus to facilitate still wider means of voyaging and wayfaring. Nevertheless this book is not a mere tissue of biographies, as a glance at the chapter titles will reveal.

The chapter on " Medicine and the Trade Routes " shows how the healing art followed the Moslem Empire in its westward march, and among other topics of interest, from which it is hard to make a selection, are " The Anatomist in Art ", " The Resurrection Men ", and " A Patient of the Renaissance ", the last-mentioned being none other than Benvenuto Cellini, appearing in a guise which may be new to some readers. One of the most interesting chapters is that which deals with the history of lithotomy and, in particular, with Mr. Pepys and a number of other

[1] [For particulars see Book Reviews.]

writers who have recorded their trying experiences as subjects of " the stone ". In the 16th and 17th centuries it was not uncommon to spread the news of a successful, or unsuccessful, operation by a broadsheet, or " Flugblatt ", as it was termed in Germany, the home of such publications. The leaflet was often illustrated by a copperplate engraving of the stone. Its weight and measurement were also given, so that we have exact pathological records of the malady, which was then so common. The illustrations of this chapter, eight in number, are perhaps the most interesting in the book, although in general the reproductions are poor, being too small and indistinct to be of real value. Nevertheless the book is so attractively written that even without the plates it would have been most pleasing. It is sure to draw many readers, and it will amply prove that in medicine a study of the past is a most useful background to the practice of the present.

Douglas Guthrie

1229

THE CHAMBERLENS AND THE MIDWIFERY FORCEPS

The story of the Chamberlens and of the invention of the midwifery forceps has often been told, but it is so remarkable that Dr. Radcliffe's little book[1] is sure of a warm welcome from all students of medical history and, indeed, from many members of the general public who will appreciate a new account of a most intriguing episode in history. So far as the Chamberlens are concerned, this book adds little, if anything, to the information provided by J. H. Aveling's book of 1882 or by such standard works as those of Herbert Spencer and Kedarnath Das ; but Dr. Radcliffe gives an extremely good account of the later development of the obstetric forceps, with special reference to the contributions of three Essex surgeons—Edmund Chapman, William Gifford, and Benjamin Pugh. The work of Smellie, John Aitken, and John Burton (" Dr. Slop " of *Tristram Shandy*) and of the french and german pioneers is also dealt with, and altogether the book provides a most concise yet readable summary of the evolution of modern instrumental midwifery. The tangled personal history of the Chamberlens, beginning with Dr. William, the founder of the dynasty, who came to England as a Huguenot refugee in 1569, is here clarified. It is probable that William's son, Peter Chamberlen I (died 1631), was the inventor of the instrument that has preserved the family name. Hugh Chamberlen, Senior, was the chief exploiter of the secret and, by virtue of his position as accoucheur at the Court and by his contacts abroad, did most to spread the use of the forceps. The forceps themselves were lost to the world for more than a hundred years prior to 1813, when four sets were discovered in a box hidden under a floorboard at Woodham Mortimer Hall, near Maldon in Essex. This house was occupied by Dr. Peter Chamberlen III in the time of King Charles II, and it appears that the instruments were hidden by his widow. The secrecy which the Chamberlens maintained in regard to the nature of their invention has been strongly condemned, and poetic justice has led some historians to attribute the invention to other obstetricians. Strong claims have been made on behalf of John Palfyn, a surgeon of Ghent; but it is known that Palfyn visited London and it is probable, as Dr. Radcliffe maintains, that he heard of the forceps through one of the Chamberlen family and devised similar instruments of his own on his return to the Low Countries. Dr. Radcliffe also gives a graphic account of Hugh Chamberlen's visit to the Hôtel Dieu at Paris and of his unsuccessful attempt to deliver one of the great Mauriceau's patients—a rachetic cripple —by means of his forceps. He also deals with Chamberlen's later days at Amsterdam, where he is said to have sold the family secret to certain Dutch surgeons.

One or two slight errors may be noticed: the ill-fated Sir Richard Croft is referred to as Crofts, and the great french obstetrician Mauriceau appears throughout as Moriceau. The very interesting Chamberlen family tree given on page 72 could well be extended by reference to Peter Chamberlen's will as printed on pages 9–14 of Aveling's book on *The Chamberlens* (1882). This gives information concerning his wife Anne Cargill. Neither Aveling nor Dr. Radcliffe mention Peter Chamberlen's son David (1590–1618), who studied medicine at Leyden, became a ship's surgeon in the East Indies Fleet, and bequeathed " fifty Jacobus pieces in gold " to Marischal College, Aberdeen (Smith, 1932).

W. J. Bishop

[1] [*The secret instrument.* For particulars see Book Reviews.]

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1230

ST. THOMAS'S HOSPITAL 1106–1947

This short account[1] of the development of one of London's most famous hospitals is intended for the layman rather than the medical historian, for in 72 pages it is not possible to do more than touch upon a few of the outstanding persons and events associated with the life of so old a hospital.

Once more the claim is made that St. Thomas's is the oldest of the London hospitals, although the author is unable to present any fresh evidence; all that can definitely be claimed is that, even before the Norman Conquest, there existed a religious establishment on the south bank of the river Thames adjacent to London Bridge, upon the site of which St. Thomas's Spital was standing in 1173. This site was continuously occupied by the hospital until the removal to Lambeth in 1871.

In so small a book it is possible to mention only a few of the medical giants who walked the hospital and taught in it in the past, but the author might have devoted a little more of his valuable space to this aspect of the life of the hospital, and less to nursing, which is very fully reported, especially in the second half of the book. Much space is devoted to the life of Florence Nightingale, even before she became connected with the hospital; of the 49 illustrations, 4 depict Miss Nightingale and altogether 10 are concerned with nursing. Of the remainder, 16 have no connexion with the hospital and only 3 consist of portraits of eminent St. Thomas's men (Cheselden, Mead and Sir Astley Cooper—the last-named incidentally being more concerned with Guy's Hospital, to which he was full surgeon). An appropriate companion portrait to that of Dame Lloyd Still would have been one of the late Sir Arthur Stanley, for so many years, and despite much infirmity, the hospital's devoted Treasurer; he is not even mentioned. Sir Cuthbert Wallace, Sir Percy Sargent, W. Rowley Bristowe (*sic*), Sir Maurice Cassidy and Sir George Makins are mentioned only by name; much could have been written about each one of them. We look in vain for a word about the Ballances, Shattock, Mellanby, Sherrington, to name but a few who spring to mind, although space is found for a story about Keats and a note on Mr. Somerset Maugham, both of whom learned their medicine at St. Thomas's but made their mark in other fields.

While it is true that no hospital has contributed more towards raising the status of nursing in this country, it has done so only during the last 80 years—since the advent of Miss Nightingale. On the other hand it has been a hospital for almost a thousand years and its physicians and surgeons have made many fundamental contributions to medical science. There should, for instance, have been room for a story of Cheselden's operation for stone; instead he is described as St. Thomas's " greatest surgeon " who " specialized in anatomy and became a leading oculist as well ".

Nevertheless, Mr. Graves gives a most interesting account of the hospital during its long life and has obviously taken great pains to verify his facts. When he approaches the period of the recent war he is on firmer ground. He gives a vivid account of the grave damage caused to the hospital by air-raids, and of the evacuation of much of the hospital and all the medical school to Surrey. He is able, too, to include some photographs showing the extent of the damage sustained, but he is quick to point out that, severely as the war has dealt with this great hospital, it has at least given an opportunity for rebuilding what was a fairly modern hospital on even more modern lines. He outlines the plans for future reconstruction and closes his story with the hope that nationalization will not affect the service of the hospital or the patients' faith in it.

The illustrations are beautifully reproduced, and 8 are in colour. In preparing the book, Mr. Graves has obviously obtained much

[1] [For particulars see Book Reviews.]

of his information from the three-volume *History of St. Thomas's Hospital*, and from *St. Thomas's Hospital Gazette*, the one written by and the other founded by, the late Professor F. G. Parsons; yet we look in vain for the author's acknowledgement to one who laboured for several years to produce the only comprehensive history of the hospital.

L. T. Morton

1231

THE STORY OF QUININE

A gaudy jacket, which promises " romance, bloodshed, and the glitter of gold " in a form comparable " to the most highly imaginative fiction ", is a truer indication of the publisher's aim than it is of the author's, and it would be regrettable if this disguise were to deter the serious reader from approaching a work which is obviously the product of considerable literary research. Our judgement of the factual basis of Mrs. Duran-Reynals' history of quinine[1] is further prejudiced by the omission of " an excellent bibliography which includes many obscure and little-known primary sources ", an item which, so Professor Fulton tells us in his preface, was included in the american edition of 1946.

This book is indeed a " pageant " rather than a history, for the author has chosen to illuminate a carefully selected series of dramatic events, each a milestone in the history of the exploitation of one of the most important drugs in the pharmacopoeia, and one which was described by Ramazzini as being capable of transforming the art of medicine as drastically as gunpowder transformed the art of war.

Introduced into Europe about the year 1639, its true value was for long a subject of violent dispute, while the fact that it was sponsored by the Jesuits brought it into the arena of religious controversy. The familiar story of Sir Robert Talbor, whose empirical use of the powdered bark won him fame and royal patronage in both England and France and secured its introduction into the official Pharmacopoeia of 1677, is followed by an account of the expedition which enabled La Condamine to give the first botanical description of the tree itself. The pitiful career of the english botanist Richard Spruce, who, on the slopes of the Andes, collected the seeds from which were grown the " red cinchona " plantations of India, the source of *totaquine*, is paralleled by the heroic gesture of the Indian, Manuel Incra, which brought eponymous fame to his master Charles Ledger (*Cinchona ledgeriana*) and led to the establishment of the great " quinine empire " of the Dutch in Java. In the concluding pages of the book we are given the story of the political and commercial hucksters, who " rigged the market " in order to maintain prices, restricting output of the previous drug while less than one-half per cent. of malaria sufferers—who comprise nearly a half of the world's population—were able to benefit from it. That is ironical enough, but it is—or was—an economic commonplace.

There is tragedy, in every sense, as well as irony, in the chequered history of cinchona, and nowhere is this so persistent and unyielding as in the career of the great south american naturalist José Celedtino Mutis, and the establishment of " The Botanical Institute of the New Kingdom of Granada " at Bogotá. This, the first genuine scientific institution in the New World, was destroyed in the violence of counter-revolution, its director, Caldas, shot as a rebel, and the whole of its scientific documents, drawings and manuscripts, including the results of Mutis's life-work, seized by spanish troops and shipped to Madrid, there to moulder unopened until the present decade. The story of this " great failure ", which is comparatively unknown in this country, is undoubtedly the most valuable chapter in this book.

The writing is of the dramatic, occasionally sensational kind, but it is not unpleasing and the historical details are generally accurate. A few errors call for correction however. The *Schedula romana*, described as " a hastily written manual ", was really a simple leaflet giving instructions for the use of the drug. The latter was first administered in England not in 1658, but certainly before 1655 by John Metford, a Northamptonshire physician whose case-book is now in the British Museum. Quinine, an alkaloid extract of cinchona isolated by Pelletier and Caventou in 1820, is confused anachronistically with the bark itself. The general medical background is hazy and sometimes wildly erroneous, as in the statement on page 71 that, in the year 1666, Harvey and Vesalius " had been officially repudiated and it is doubtful whether the rank-and-file practitioner knew much about them."

However, if Mrs. Duran-Reynals has not given us the substantial work of irreproachable scholarship which the history of cinchona merits, we must acknowledge that she has written the most lively and stimulating sketch yet offered to the public.

F. N. L. Poynter

[1] [*The fever bark tree.* For particulars see Book Reviews.]

1232

ANONYMUS LONDINENSIS

Anonymus Londinensis is the name given to a medical papyrus in the British Museum. It was first described by Sir Frederick Kenyon in 1892. An elaborate edition of the greek text was brought out by Hermann Diels in the following year, and a german translation, with notes, by Heinrich Beckh and Franz Spät was published in 1896. The papyrus probably dates from the second century A.D., and represents a copy, made for private use, of an earlier work. In this edition[1] the greek text of Diels has been reprinted together with an english translation, based on an amended text, and valuable notes. Dr. W. H. S. Jones, President of St. Catherine's College, Cambridge, who is responsible for the present work, is a classical scholar who has for many years made a special study of greek medicine. He is already well known to medical historians as the author of a monograph on *Malaria and greek history* and as co-editor, with the late Dr. E. T. Withington, of the Loeb Hippocrates. The translation is the part of the book to which Dr. Jones has devoted practically his whole attention. The original is full of almost insuperable difficulties, and few more competent authorities could have been found to undertake their solution.

The work known as *Anonymus Londinensis* consists of over 1,900 lines, and is divided into three parts, dealing with (1) definitions, (2) the etiology of disease, and (3) the history of physiology. A great part of the work appears to have been taken from the *Menoneia*, a collection of medical opinions attributed by some to Aristotle, but really written by Aristotle's pupil Menon. Some authorities think that the original of *Anonymus* was a series of extracts made by a student from Alexander Philalethes, a pupil of Asclepiades, who flourished at the beginning of the 1st century A.D., and is the latest authority mentioned in the text. Another theory, maintained by Max Wellmann, is that the author was Soranus of Ephesus, a physician of the 2nd century A.D. and a leading authority on midwifery and the diseases of women. The conclusion of Dr. Jones is that the papyrus is a copy, made by a medical student, of lecture-notes also made by a student, and containing elements derived from all the above-mentioned sources.

The first part of the work deals with the definition of such terms as " life," " soul," " bodily affection," and " psychic affection." Part two is concerned entirely with the causes of disease, which are reduced to two classes: (1) residues from food, and (2) disturbances in the blendings of the elements composing the body. Of the twenty medical authorities quoted, seven were unknown before the discovery of this papyrus. This section also contains a long account of Plato's medical views. The third section deals with the history of physiology after 300 B.C., from Herophilus to Alexander Philalethes, and is the most interesting as regards subject matter. A brief account of human anatomy is followed by a discussion of ideas of vitality and motion, nutriment, and the various emanations from the body. Special attention is paid to digestion, to the veins and arteries, and to the invisible " pores ". According to Dr. Jones, certain statements in *Anonymus* provide the only reliable testimony for the doctrine of the historical Hippocrates, a point of considerable importance in view of the sceptical attitude which now prevails in regard to the works of the Hippocratic *Corpus*. Many of the problems posed by *Anonymus Londinensis* may never be finally settled, but as Dr. Jones remarks, " the Hippocratic problem, like the Homeric problem, cannot take from us our heritage."

In two supplementary essays Dr. Jones deals with the nature of greek thought and the nature of greek medicine, and gives a masterly exposition of the relations between medicine and philosophy in the ancient world.

W. J. B.

[1] [*The medical writings of Anonymus Londinensis.* For particulars see Book Reviews.]

Book Reviews

ALLERGY

1233 Synopsis of Allergy

Harry L. Alexander. Second Edition, London, Henry Kimpton, 1947. 255 pages ; 22 figures. 20 x 13 cm. £1

(i) Historical; (ii) atopy; (iii) bronchial asthma; (iv) hay fever; (v) atopic rhinitis; (vi) gastrointestinal allergy; (vii) headache, conjunctivitis, other atopic disorders; (viii) allergic dermatoses; (ix) physical allergy; (x) drug allergy; (xi) serum allergy; (xii) bacterial allergy; (xiii) vascular allergy. Appendix. References.

Since the first edition of this book was published, the introduction of anti-histamine drugs has opened up a promising line of advance in the therapeutic field in allergic disorders. It may be that this fact has given to the physician an added interest in allergy. Many of the books written on the subject tend to be overburdened with the theoretical aspects rather than the known facts. A small book such as Professor Alexander has produced should satisfy the needs of a large number of people who require an up-to-date review of the modern trends of knowledge in the allergic disorders.

The author begins the book, after a brief historical survey, with some general considerations of allergic diseases. He stresses throughout the book the possible limitations of the skin test, which is of value so long as the limitations are understood. The differentiation of asthma into what is called atopic and intrinsic may be new to some workers. In atopic asthma there is often a positive personal and family history of atopic disorders and the skin tests are usually positive. This type, which usually begins in the 1st or 2nd decade, may react to environmental control. Intrinsic asthma on the other hand usually has no family or personal history of atopic disorders, the skin tests tend to be negative, the age of onset is after the second decade and the prognosis, even with proper treatment, is uncertain. The chapter on asthma has a lot of sound advice on possible lines of treatment.

The section on hay fever is the best in the book. In the USA the importance of ragweed as well as the grasses, as a cause of hay fever, may make it necessary for the patient to start treatment in February and continue until September. It is not surprising therefore that the author considers perennial treatment gives better results than pre-seasonal. Co-seasonal treatment is considered an emergency treatment rather than one of choice. More recent works, since this was written, suggest that co-seasonal treatment with a suitable anti-histamine drug gives results that are as good as any other method used.

The last nine chapters of the book deal with other aspects of allergy not related to asthma or hay fever. It is impossible in a synopsis not to be dogmatic, but even those workers whose opinion the author does not share are given more than adequate mention. In a book where such a wide field of knowledge is covered there are sure to be some gaps. The index is not full enough. A better photograph than that shown of atopic dermatitis should be found. British readers will be surprised to find no mention of the Noon unit in the standardization of extracts.

However, these are minor criticisms. The book can be strongly recommended as an easily-read account of modern ideas in allergy. There is a short list of references at the end of the book for those who require a more-detailed knowledge of allergic work.

A. W. Frankland

ANAESTHESIA

1234 A Synopsis of Anaesthesia

J. Alfred Lee. Bristol, John Wright & Sons, Ltd., 1947. vi + 254 pages ; 42 illustrations. 19 × 13 cm. 12s. 6d. [£0.625]

(i) Notes on the history of anaesthesia; (ii) respiration; (iii) pre-anaesthetic care and preparation; (iv) premedication; (v) inhalation anaesthesia; (vi) agents for inhalation anaesthesia; (vii) the closed circuit; cyclopropane; controlled respiration ; (viii) nitrous oxide anaesthesia; (ix) accidents of inhalation anaesthesia and how to treat them; (x) gases used in association with anaesthesia; (xi) endotracheal anaesthesia; (xii) rectal anaesthesia—basal narcosis; (xiii) intravenous anaesthesia; (xiv) analeptics; (xv) spinal analgesia; (xvi) regional anaesthesia; (xvii) refrigeration analgesia; (xviii) choice of anaesthetic as influenced by type of operation; (xix) choice of anaesthetic and methods as influenced by general condition of patient; (xx) the use of curare in anaesthesia; (xxi) shock; (xxii) anaesthesia in thoracic surgery; (xxiii) the complications and sequelae of anaesthesia; (xxiv) explosion risks in anaesthesia; (xxv) management of the unconscious patient; (xxvi) anaesthetic records; (xxvii) anaesthesia and analgesia in labour. Index.

This book would appear to be as good as any synopsis can be. It contains a précis of all the essentials of anaesthesia and analgesia, presented with a balance and lack of bias which is most refreshing.

Any book of this nature is meant for the student who has already read through a textbook and who has a sound knowledge of the subject by practical experience. He can then use it to revise any section quickly or to look up any facts or figures which he may have forgotten. On the other hand, the limitations of a synopsis should also be realized. The matter presented must of necessity be largely composed of stark statements without explanations or references. It is thus unsuitable for the novice and must not be regarded as a " cram-book " which offers an easy short-cut to knowledge.

The production of the book is excellent and the use of many different types breaks up the pages in an agreeable manner.

Proof-reading must have been exceptionally thorough, as only one error was detected by the present reviewer. On page 131, the strength of the intravenous drop of adrenaline is given as 1 in 125,000 instead of 1 in 250,000.

The book can be recommended without reserve to the class of reader for whom it is written.

C. Langton Hewer

1235 Curare : its History, Nature, and Clinical Use

A. R. McIntyre. Chicago, The University of Chicago Press; London, Cambridge University Press, 1947. vii + 240 pages; 25 illustrations. 25 x 17 cm. £1 7s. 6d. [£1.375]

(i) Curare and its meaning; (ii) the early history of curare; (iii) the first witnesses; (iv) botany; (v) chemistry; (vi) early experiments with curare; (vii) the actions of curare on nerve and muscle; (viii) theories of curarization; (ix) effects of curare on the circulation and respiration; (x) effects of curare on the viscera; (xi) absorption, excretion, and toxicity of curare; (xii) miscellaneous effects of curare; (xiii) curare and the central nervous system; (xiv) the clinical use of curare; (xv) conclusions and speculations. Addendum. Subject index. Author index.

This is an authoritative monograph sponsored by the University of Chicago Committee on Publications in Biology and Medicine; the author is Professor of Physiology and Pharmacology at the University of Nebraska.

The history of the discovery of the south american arrow poison is narrated with meticulous accuracy and with frequent quotations from the pioneer naturalists.

The various plants from which the crude curare has been extracted are fully described and illustrated in the chapter entitled Botany.

The pharmacological effects of the alkaloid on the various systems of the body are described in great detail and incorporate the research work carried out by the author with his colleague Dr. A. E. Bennett over a period of six years. It is interesting to note that Dr. McIntyre does not regard the electrical and biochemical theories of neuromuscular transmission as being antagonistic but complementary.

Only one chapter is devoted to the clinical use of curare and only four pages to its applications in anaesthesia but nevertheless the book is probably the most exhaustive source of information extant about the drug as a whole and can confidently be recommended.

C. Langton Hewer

CANCER

1236 Cancer of the Breast

Duncan C. L. Fitzwilliams. London, William Heinemann Medical Books, Ltd., 1947. vii + 199 pages ; 24 illustrations. 22 x 15 cm. £1 5s. [£1.25]

(i) The nature of the disease; (ii) spread of cancer; (iii) early diagnosis; (iv) clinical signs; (v) etiology and pathology; (vi) the treatment of carcinoma: early cases treated by local removal; (vii) treatment by operation; (viii) treatment by radium; (ix) treatment of late cases; (x) clinical types; (xi) other forms of treatment; (xii) X-ray therapy in carcinoma of the breast. Index.

The author expounds here in colloquial language his own ideas and experience of mammary cancer, and amplifies the text by case-notes. His advocacy of a more restricted operation than was the former custom is of particular value. In the past, surgeons have tried to overtake the spread of cancer by ever widening the field of operation. Modern inquiries, however, have shown that *x* rays can deal with the remoter extensions of cancer better than surgery alone; and radiotherapy after operation is therefore coming rapidly into general and effective use. The case-notes properly record mistakes occasionally made by the general practitioner or the surgeon when consulted by a patient with cancer of the breast. Tragic errors sometimes occur in this difficult field and the more that is known about them the less often will they happen. Procrastination is a great evil. Once cancer has begun it must be presumed to be spreading all the time, and the need for treatment is urgent. Mr. Fitzwilliams mentions the delay caused either by the patient's reluctance to consult her doctor, or by the doctor's hesitation to refer her to a surgeon; but he gives little attention to the prolonged interval which so often elapses between the advice to undergo an operation and its performance. This at present is part of a troublesome national problem, because of the paucity of hospital accommodation, and any detailed information about it would be acceptable.

Apart from the useful case-notes and description of surgical technique, the book contains several dogmatic statements which are questionable, and in some instances appear to the reviewer to be misleading. This comment may be illustrated by the quotations which follow :—

> I remember reading of some experiments which showed that if carcinogenetic substances were painted on the skin of an animal and a carcinoma established, and if that carcinoma was excised locally before dissemination had taken place, no subsequent painting of the skin would start a similar carcinoma. If this is true, the laboratory bears out what we see clinically, and leads us to believe that the growth of one carcinoma confers an immunity on the host against another similar growth starting.

Referring to involvement of the lymph nodes he states:

> It should be realised that the importance of the lymphatic stage was only established at the beginning of this century . . .

Although the spread of cancer by the blood-stream has been known for more than a hundred years we are told that

> . . . the clinicians have so far failed to realise its significance. The teaching in most medical schools remains much the same as when I was a medical student, namely, that sarcoma spreads by the blood stream, but carcinoma spreads by the lymphatics.

Discussing early diagnostic signs and referring to retraction of the nipple, he states:

> This is a useful help in diagnosis, though unfortunately it is absent in the majority of cases.

And in a brief discussion on etiology, we read:

> When our accepted theories of heredity have been so shaken by the recognition of the doctrines of Mendel, it is very difficult to be positive about heredity.

After mentioning the milk factor of mammary cancer in mice, he says:

> In any case so few human mothers now suckle their offspring that the matter is hardly worth considering.

The illustrations on pages 87 and 88 and facing page 92, showing suggested arrangements of radium needles for the treatment of mammary cancer, appear to the reviewer to disregard the principles of dose-distribution on which such treatment must be founded.

An excellent chapter on the principles of *x*-ray therapy by Dr. Alice Ross is an addendum to this little volume.

Though it can be recommended to surgical technicians of experience who can form their own judgements, the book contains so many questionable statements that it cannot be regarded as a sound guide to the student or as an accurate exposition of the science of british surgery.

Harold Burrows

1237 Bioterapiya Zlokachestvennikh Opookholay

N. G. Klueva & G. I. Roskin. Moscow, Akademia Meditsinskych Naook, 1946. 224 pages; 97 figures; 19 tables. 22 x 15 cm.

(i) Introduction. (ii) Inhibitors of malignant growth: mouse carcinoma and human carcinoma; general remarks on tumour-inhibiting substances; metals, lead; dyes as chemotherapeutic substances; heptylaldehydes; carcinogenic hydrocarbons; immunotherapy; yeast. (iii) Bacterial products: mode of action; experimental and clinical studies on polysaccharides from *B. prodigiosus*. (iv) The action of toxins from *Corynebacterium diphtheriae* and *B. tetani*: treatment of transplantable tumours; treatment of spontaneous mouse tumours by diphtheria toxin. (v) Protozoan infections and transplantable tumours: *Trypanosoma cruzi* infection and the growth of transplantable tumours; the specificity of *T. cruzi* action on transplantable tumours; the effect of *T. cruzi* and other protozoan endotoxins; *T. cruzi* and transplantable sarcoma; trials with " K-R " substance; the active part of the " K-R " substance; trypanosoma vaccines; vaccines prepared with alcohol, with metaphen; products obtained by lysis of *T. cruzi*; experiments with the " K-R " substances of the 3rd, 4th and 5th modifications. (vi) Histological and cytological changes in tumours induced by the carcinolytic substance: the action of *T. cruzi* on Ehrlich adenocarcinoma and Crocker sarcoma; the effect of the " K-R " substance on Erhlich carcinoma and on spontaneous tumours in mice; histological and cytological changes in Crocker sarcoma induced by *T. cruzi* and the " K-R " substance. (vii) Summary and conclusions from experimental investigations. (viii) Preliminary clinical studies on the anti-tumour substance from *T. cruzi* (" K-R " substance): the purpose of clinical trials; description of cases; modifications of the " K-R " substance employed in clinical trials; carcinolytic syndrome; carcinolytic reaction and regeneration of normal tissues; the possibility of a cancer cure by the sole application of the " K-R " substance; the lytic reaction in various types of tumour tissue; induction of resistance in tumour cells and susceptibility of the body after repeated application of the " K-R " substance; relationship between the dose and the lytic reaction in tumours; mode of application of the " K-R " substance; subjective reaction after inoculations; local reaction; temperature; blood pressure; cardiovascular reaction; general reaction; preliminary results. (ix) Anti-tumour substance of *T. cruzi*: tropism and antagonism; properties of the anti-tumour substance from *T. cruzi*; mode of action of the " K-R " substance; treatment of Brown-Pearce carcinoma and its significance. (x) Conclusions. (xi) 133 References.

This is a monograph on the experiments carried out by Roskin and his collaborators on treatment of tumours with various bacterial and protozoal products.

It is felt that of the two main duties of the reviewer, description and criticism of the work, the first should receive foremost consideration in the present case. Hence an attempt will be made to acquaint the reader with the main points in the experiments and with the results described.

The book is divided into two parts. In the first, experimental, and in the second, clinical work is described.

The first part, preceded by a fairly comprehensive review of the many attempts to inhibit malignant growths, can be subdivided into a chapter devoted to the studies on treatment of tumours with diphtheria- and tetanus-toxins and a chapter on protozoan infections and tumours.

The treatment of transplantable Ehrlich carcinoma in mice with B. tetanus toxin gave complete regression of tumours in 19 out of 48 mice, and inhibition of tumour growth in 6 more mice, with an average decrease in tumour weight of about 5 times that of the control mice. Similar results were obtained with Flexner-Jobling carcinoma in rats and with Kritchevsky-Sinelnikov sarcoma in rats. Better results are claimed in the treatment of Ehrlich carcinoma with diphtheria toxin, where the dose and concentration play an important part. While treatment of Ca63 carcinoma in mice was disappointing, in Crocker's sarcoma the weight of treated tumours was 4 times smaller than that of the controls. The authors claim that diphtheria toxin inhibits the growth and induces the disappearance of tumours in a large percentage of animals, even in well-established tumours (of ten days' growth).

Diphtheria toxin was also employed in the treatment of 40 mice with spontaneous mammary tumours of various sizes. Unfortunately, the strain of mice is not mentioned, nor is the age of the tumours. Complete regression of tumours was recorded in 15 mice, diminution in tumour size in 18 mice, complete inhibition of tumour growth in 6 animals. It is a matter of regret that neither controls, nor data about the life-span of mice in which the tumours regressed, or the dosage employed, are mentioned. The experiments are accompanied by numerous drawings of mice with tumours and their progressive decrease in size is presented. The effect of the treatment is rapid: usually 7–14 days are sufficient to give complete regression of tumour growth. There are no histological descriptions of changes in tumour tissue induced by the treatment.

In the fifth chapter, on protozoan infections and tumours, experiments are described which date back to 1931. They were mostly carried out on mice with implanted Ehrlich adenocarcinoma. In an experiment in which 45 mice (strain not given) were infected with *T. cruzi* and at the same time implanted with Ehrlich carcinoma, the tumours disappeared in 30 mice, and tumour growth was greatly retarded in the 15 remaining mice. All the test mice eventually succumbed to the infection, but they lived longer than the control mice or the mice infected with *T. cruzi* but not implanted with tumours. In order to investigate the specificity of the *T. cruzi* effect on tumours, *Spirochaeta duttoni* and *Spirochaeta obermeieri* were tested against Ehrlich carcinoma, and *T. equiperdum* against a guinea-pig carcinoma (strain not stated), but they had no influence on tumour growth. The authors consider, therefore, the effect of *T. cruzi*

on tumours to be specific and not merely the result of nonspecific fever therapy. An endotoxin prepared from serum of mice infected with *T. cruzi* gave in mice with Ehrlich carcinoma results similar to those obtained with living trypanosoma, and had the additional advantage that none of the treated mice died from infection. Serum from healthy mice had no effect on tumours. The injections were given each time on the opposite flank to that in which the tumour was grafted. Endotoxins from *T. equiperdum*, *T. gambiense*, *T. lewisi*, and from *Leishmania tropica* and *Proteosoma praecox* had no influence on tumour growth. Small pieces of Ehrlich carcinoma placed in drops of serum containing *T. cruzi* endotoxin and kept for six hours at 14–15° C. gave no tumours when implanted into mice, while control pieces treated with normal serum induced tumours in mice. Thus the authors maintain that the endotoxin has a direct toxic effect on tumour tissue and an indirect effect on the reticulo-endothelial system, because the endotoxin was ineffective and lethal to the majority of animals when the reticulo-endothelial system of tumour-bearing mice was blocked by splenectomy or by various chemical means. The positive effect was also obtained in rats with implanted Flexner-Jobling carcinoma. It seems that the use of nonhomozygous animals could easily be a subject of criticism; on the other hand the significance of the results described may appear to be greater if they were obtained with nonhomozygous animals. It is a pity that in no case the strain of animals is mentioned.

The experiments interrupted owing to the outbreak of war were started again in 1944 on transplantable Crocker sarcoma and Ca63 adenocarcinoma in mice. Experiments with Ca63 were disappointing as it grew rather slowly, and the influence of live *T. cruzi* could not be investigated. In three experiments comprising 28, 14, and 29 mice respectively, implanted with Crocker sarcoma and injected with *T. cruzi* 9 days later, the tumour growth was greatly retarded, and in some mice the tumours disappeared. Postmortem examination of tumours showed considerable development of connective tissue with large necrotic areas. Histological examination showed necrosis of tumour tissue with connective-tissue development.

A substance obtained from plasma of mice infected with *T. cruzi* heated at 50°C. for 20 minutes, and described as " K-R ", was injected in daily doses of 0.5 cm.³ during 1 month into mice, implanted several days previously with Crocker sarcoma and Ca63, and induced the regression of tumours in about 60 % of the treated mice.

In an attempt to obtain the active substance, plasma of mice infected with *T. cruzi*, from which trypanosoma were removed either by centrifugation or by filtration through Berkefeld candles, was found to be ineffective. *T. cruzi*, however, obtained by centrifugation from the blood of mice, treated with alcohol (1 part to 9 parts of physiological saline) for 24 hours in the ice-chest, and resuspended in physiological saline, induced the disappearance of Crocker sarcoma in all of the treated mice. Regression or inhibition of Ca63 was also obtained with *T. cruzi* treated with metaphen. The authors conclude that alcohol and metaphen do not destroy the anti-tumour substance. Plasma of mice infected with *T. cruzi*, treated with bidistilled water for 24–48 hours in the ice-chest, then filtered through Berkefeld filters, was injected daily in 1 cm.³ doses into mice implanted with Ca63 and Crocker sarcoma. The tumours disappeared in 60 % of the treated mice. The authors point out that the anti-tumour substance is filterable and remains active although *T. cruzi* undergo lysis. All these substances are described as modifications of the " K-R " substance with various consecutive numbers. The " K-R " substance of the so-called 4th modification (double strength) was injected subcutaneously in 0.5 cm.³ doses into two mice with spontaneous breast carcinomata. In one mouse (strain not stated) there was no effect, in the other after 20 injections the tumour growth was greatly retarded and the postmortem examination revealed a small nodule consisting of a large area of necrosis but with living tumour cells present.

The authors found *T. cruzi* in all organs of normal mice, while in mice with implanted tumours they could be found only in the tumour cells which in consequence undergo degenerative changes. A number of photographs illustrate the degenerative changes in transplantable tumours induced by the " K-R " substance. The protozoa are believed to contain a specific carcinolytic substance which is filterable, dialyzable, can be preserved in dried state, and is harmless to the animals. This observation led to clinical trials with this substance which are described in the second part of the book.

The " K-R " substance was tried on 57 human cases, during 1939–1941 and during 1945–1946. In 4 cases the application of the " K-R " substance was successfully completed; in 27 cases it was interrupted either because of no improvement or for various other reasons, and 26 cases were still being treated. The maximum number of injections given varied from 30–200, each comprising from 10–30 units of " K-R " substance in 1 cm.³ (1 unit containing the active substance from 3 millions of *T. cruzi*). The number of units in one injection varied from 500 to as many as 2,000. The substance was given either by subcutaneous or intramuscular injections; quite recently the intravenous route has been used. Complete disappearance of tumours followed by connective-tissue reaction is claimed in four cases: carcinomata oesophagi, recti, mammae, and laryngis; improvement is described in four similar cases, and in carcinoma of the lips. The authors stress the lytic effect in carcinoma combined with the complete destruction of the tumour tissue. The lytic effect was in some cases already apparent after 10–15 injections, in others after 30 injections. No toxic symptoms or cachexia following the treatment were observed. It is to be regretted that the photographs of changes in the tumours are of poor quality so that it is very difficult to assess them. The authors stress that there are no side effects even after the largest doses of the " K-R " substance, but it is rather surprising to hear that there is no necessity at all to use other forms of treatment. The authors describe only local pains of short duration in the tumour region with no reaction at the site of injection. As regards general reaction, shivers with pains in the joints, followed by a rise of temperature to 102°F., lasting only a few hours, were usually observed. The examination of blood showed no pathological changes except a passing increase in eosinophils. Cardiovascular reaction was recorded in only two cases and was of a passing character.

The authors also describe the disappearance of metastases and inhibition of tumour growth in Brown-Pearce carcinoma in rabbits treated with the " K-R " substance. Histochemical analysis of cells from tumours regressing under the treatment has shown a decrease or disappearance of ribonucleic acid. The authors presume that the " K-R " substance may interfere with the synthesis of proteins or block the enzyme systems connected with the synthesis of proteins.

It must be pointed out that the difference between transplanted tumours and tumours derived from the tissues of the animals (spontaneous and induced by various means) has been the basis of many premature descriptions of successful experimental treatment of tumours. Transplanted tumours have been " successfully " treated by various means but the extension of the work to spontaneous tumours in every case has given disappointing results. Therefore any results obtained with transplanted tumours must be considered as unproved until carried out with naturally-occurring tumours. From this point of view the work of Roskin and his school requires extension and verification. It is difficult to appraise the results in patients owing to the short time of observation.

The recent revival of interest in the therapeutic effects of bacterial metabolites, first described over 50 years ago by Coley, the isolation of the haemorrhage-inducing polysaccharide from filtrates of *Serratia marcescens* cultures, and the difference in the response of malignant and normal tissues to this polysaccharide should give additional interest to the results described by Roskin and his co-workers. Finally it should be mentioned that in a joint institutional programme of the National Institute of Health and the Lankenau Hospital Research Institute, the repetition of Roskin's work has been included. These results are eagerly awaited, and should they be confirmed, the identification of the active substance will have to be the next step in this arduous line of research.

L. Dmochowski

1238 Regional and Local Differences in Cancer Death Rates

Percy Stocks. London, His Majesty's Stationery Office. 1947. (General Register Office, Studies on Medical and Population Subjects, No. 1.) 46 pages; illustrations. 24 x 15 cm. 1s. [£0.05]

The Registrar-General for England and Wales introduces, with this Report, a new series of publications under the general heading of " Studies on medical and population subjects ". The

object of the series is to provide more-detailed analyses of important subjects than is possible in his Annual Statistical Reviews.

Dr. Stocks begins his study with a review of cancer mortality rates in various countries and the inferences made from them by previous writers on the subject. Marked differences occur between different countries in the mortality levels for cancer of certain sites, and the hypothesis that these can be explained by over-certification or incomplete certification in some countries is examined. Variation in mortality levels, however, is also to be observed within individual countries and this paper is primarily concerned with such variation in England and Wales.

Records of deaths over the last twenty years reveal that mortality from cancer of the stomach has shown little change amongst men between the ages of 45 and 64, but above this age the rate has increased by approximately 5%. Amongst women, on the other hand, stomach cancer has decreased generally. For all other sites combined the male rate has increased by 6 to 9%, compared with a decrease in the female rate of some 6%. Interesting features of the trend of lung cancer are the difference between the sexes, mortality having increased twice as much amongst men as amongst women; and the very great increase in certified mortality from this cause—the male rate being six or seven times as great now as it was twenty years ago.

For certain organs of the body important differences exist in mortality levels between administrative and geographical regions; for example, the proportion of deaths assigned to cancer of the respiratory organs to those of all sites is higher in London and the County Boroughs than in the Rural Districts. For cancer of the stomach, on the other hand, the position is reversed.

A significant correlation was found between comparative mortality from cancer of the stomach and certain environmental indices ($r = 0.543 \pm 0.129$ with "persons per room" and $r = 0.526 \pm 0.132$ with the "social class index") when the rates for males aged 45–64 in 30 large towns were examined. Cancer of the lung, in contrast, was not associated with environment in this way. Cancer mortality from 1921–30 amongst women aged 45–64 revealed that the highest comparative mortality (from cancer of the ovary, 116), and the lowest from cancer of the stomach, 82) were associated with the best social conditions. At the other end of the scale, the highest comparative mortality (from cancer of the stomach, 124 and uterus, 110), and the lowest (from cancer of the breast, 90 and ovary, 77), were associated with the worst social conditions.

Only the more striking correlations and contrasts have been mentioned above. In the sections on variations in mortality from certain sites, between social classes, environmental groups and other factors in England and Wales, Dr. Stocks discusses many interesting results, a full enumeration of which is not possible here. However, it is perhaps of interest to record the high negative correlation ($r = -0.690 \pm 0.117$) found between mortality from lung cancer and hours of sunshine from the data of 20 towns.

The Metropolitan Boroughs of London provide a useful source of mortality data for an analysis of this nature in that a fair degree of uniformity of diagnosis, treatment, and climatic conditions is common to all. Further correlations revealed that amongst males aged 45–64 both cancer of the stomach and cancer of all sites except the stomach and lung were again highly and significantly associated with "persons per room". Again, cancer of the lung did not reveal this association. For women aged 45 and over, the standardized mortality rates from cancer of the stomach were highly correlated with the housing index ($r = 0.715 \pm 0.094$), but with the same environmental index a high negative correlation ($r = -0.779 \pm 0.074$) was found with cancer of the breast.

Mortality from some sites varied considerably between neighbouring boroughs in London and interesting contrasts emerged when the boroughs were grouped according to their source of water supply but "the curious correspondence in certain respects between cancer death rates and the sources of water does not prove that there is a causative connection".

In a foreword to the report the Registrar-General quotes the author as follows: "the purpose of this report is to present the statistical facts and point out any peculiarities in distribution and correspondences with other measurable factors which appear, so that all possible clues may be followed up by further study . . ."

There is no doubt that this report achieves its purpose and it sets out the statistical facts in great detail.

E. A. Cheeseman

1239 Entstehung und Früherfassung des Portiokarzinoms

Hansjakob Wespi. Basel, Benno Schwabe & Co., 1946. 183 pages; 95 figures. 23 × 16 cm. Sw. fr. 18.

(i) Problemstellung; (ii) Historisches zur kolposkopischen Methodik und Diagnose und zur Kenntnis der Frühformen des Portiokarzinoms; (iii) die histologischen und kolposkopischen Bilder der normalen und pathologischen Portio; (iv) Grundsätzliches zur Frage des beginnenden Karzinoms; (v) die Einteilung und Nomenklatur des Portiokarzinoms und der übrigen Portioveränderungen. 1. Teil. Die Früherfassung des Portiokarzinoms. (i) Einleitung; (ii) das beginnende und das ganz kleine Portiokarzinom; (iii) kolposkopische Erfahrungen am fortgeschrittenen Karzinom; (iv) Statistisches zur Frage der Krebsfrüherfassung; (v) Schlussfolgerungen. 2. Teil. Die Entstehung des Portiokarzinoms. (i) Einleitung; (ii) die verschiedenen Formen des Portioepithels und ihre Beziehung zum Karzinom; (iii) Beobachtungen zur Frage der Krebsentstehung; (iv) Schlussbetrachtungen. Literaturverzeichnis.

The early diagnosis and treatment of malignant disease is, without doubt, the most important problem in clinical practice today. The cervix of the uterus is exceptional amongst the common sites for the development of carcinoma because it can be examined visually without much inconvenience to the patient. It is obvious on theoretical grounds that if the cervix of a patient is examined sufficiently frequently the origin and development of carcinoma of the cervix should be traced. Hinselmann's technique of examination of the vaginal portion of the cervix under binocular vision at a magnification of about 10 diameters, combined with the reaction of the epithelium to such chemicals as iodine, acetic acid, silver nitrate and salicylic acid, was soon shown to be of great value in the interpretation of pathological changes. Much credit is due to Hinselmann for his description of the different types of epithelium and for his Rubrik system of histological types.

Dr. Wespi, working in the University of Zurich, has used Hinselmann's methods for many years and has collected together in this small volume some valuable and excellent results. If gynaecologists learnt the contents of the book and if they employed the Hinselmann technique, they should be able to diagnose carcinoma of the cervix in its earliest stages almost with precision. Not only that, but they should be able to identify suspicious areas which are now known to be precancerous in character, when the cervix should be removed by simple amputation. Indeed, if the Wespi-Hinselmann methods were used extensively, the incidence of carcinoma of the cervix would be reduced and cancer cases would be available for treatment in their earliest stages. The book is of very great value in addition to its application, for it contains an almost complete summary of the literature, and the theoretical problems are considered both in a scholarly manner and in sufficient detail. These problems are notoriously of immense difficulty, yet Dr. Wespi approaches them courageously and gives a reserved judgement when final proof is not available.

Dr. Walter Schiller has written to the reviewer to record his high appreciation of Wespi's book, and to say that an effort is being made to have the book translated and published in the USA. Without doubt it is one of the most important contributions that has yet been made to the study of early carcinoma in the human subject.

CARDIOVASCULAR SYSTEM

1240 Die Klinik der energetisch-dynamischen Herzinsuffizienz

Robert Hegglin. Basel, S. Karger, 1947. 120 pages; 82 illustrations. 24 x 17 cm. Sw. fr. 19

(i) Einleitung; (ii) die energetisch-dynamische Herzinsuffizienz als Problem; (iii) die Festellung der energetisch-dynamischen Herzinsuffizienz; (iv) experimentelle Untersuchungen; (v) Vorkommen der energetisch-dynamischen Herzinsuffizienz in der Klinik; (vi) die klinische Symptomatologie der energetisch-dynamischen Herzinsuffizienz; (vii) die prognostische Bedeutung der energetisch-dynamischen Herzinsuffizienz; (viii) die Ursachen der energetisch-dynamischen Herzinsuffizienz; (ix) die Therapie; (x) Schlussbetrachtungen. Literaturverzeichnis.

The steady advance in cardiological research leads to increased emphasis on the dynamic events in the heart. During the last decade the techniques of determination of cardiac output have

undergone rapid development. When these have been combined with pressure measurements within the heart, remarkable revelations have occurred. For example, we now know that the signs of heart failure may be present when the resting cardiac output is normal or high, and we have also acquired useful quantitative ideas on the degree to which the pulmonary arterial pressure is raised in emphysema. The field of cardiology is no longer limited by the anatomical boundaries of the heart.

Dr. Hegglin has produced a book which will interest all who wish to consider deeply the problem of the failing heart. He discusses the modern physiology of muscular contraction and points out that fatigued muscle has long been known to contract and relax slowly. If the failing heart reacted in this manner, we should expect prolongation of systolic contraction, which would show itself by an increased interval between the first and second sounds and a prolonged QT interval in the electrocardiogram, assuming that the electrical events in the ventricle were closely correlated with the mechanical. Most ordinary forms of heart failure, however, do not show prolongation of the QT interval with the exception of some cases of hypertension. Some forms of circulatory failure may show a heart reacting somewhat differently. Systole may be shortened, leading to a diminution of the interval between the first and second sounds, but this shortened mechanical systole may be followed by delayed relaxation shown in a prolonged QT interval. Dr. Hegglin has made an extensive study of the duration of systole in experimental conditions and also in a variety of clinical states. He finds, for example, that the QT interval may differ quite significantly from the interval between the first and second sounds recorded graphically, and this is quite pronounced in diabetic coma, where mechanical systole seems to be very considerably shorter than electrical systole. A similar state of affairs is seen in hepatic coma and in severe alkalosis. These conditions may be associated with a low blood potassium. Hypocalcaemia leads to prolongation of the QT interval and simultaneous lengthening of mechanical systole. Discrepancies between mechanical and electrical systole are also seen in pneumonia, septic conditions generally, Addison's disease, and hyperthyroidism.

This syndrome, which he calls energetic-dynamic insufficiency, is characterized by the absence of venous congestion, and the short interval between the first and second sounds may be recognizable on auscultation. Pulse is often rapid and small in volume, with a reduced blood pressure, and the heart size is normal.

The author discusses in detail the possible significance of all these findings. Certain similarities with veratrine poisoning are indicated. In relation to the chemistry of muscular contraction he points out the importance of potassium in the release of energy from adenosinetriphosphate, and recommends giving saline infusions and potassium chlorate (4 g. daily) by mouth in treatment.

This is a refreshing monograph, with factual detail closely argued and full of interest. It is gratifying to see attention being paid to the heart in a variety of metabolic disturbances. Such work is likely to break down the artificial barriers enclosing the "specialities" and to compel attention to the integrated physiology of the whole organism, which is the real province of the physician.

J. McMichael

1241 The Peripheral Circulation in Health and Disease. A Study in Clinical Science

Robert L. Richards. London, E. & S. Livingstone, Ltd., 1946. xii + 153 pages; 104 illustrations. 25 x 18 cm. £1 1s. [£1.05]

(i) The anatomy and physiology of the peripheral vasomotor system; (ii) methods of study—with particular reference to the recording of skin temperatures; (iii) spontaneous variations in vasomotor activity; (iv) imposed variations in vasomotor activity; (v) occlusive vascular disease; (vi) the Raynaud phenomenon; (vii) peripheral nerve injuries; (viii) the immersion foot syndrome. Conclusion. Index of authors. General index.

In this monograph concerning the peripheral vascular system, Dr. Richards assembles information that he has gained as a result of clinical observations carried out to a large extent on cases with war-injuries. This is a study in clinical science, and no reference is made to treatment.

He deals in some detail with the anatomy and normal physiological responses and vasomotor reflexes of blood-vessels, and thereby indicates how they may be employed in assessing the circulation in a limb and the way in which they may be disordered in disease. As he rightly points out, no one clinical test is adequate by itself, and he stresses how, for example in the lower limb, reflex vasodilatation may not take place when the upper limbs are immersed in hot water even though the circulation be within normal limits.

He has also much to add that is of interest in the interpretation of skin-temperatures. His study of vascular changes associated with peripheral nerve injuries is instructive. He believes that tropic changes, formerly thought to be a specific sequel to division of peripheral nerves are, in fact, largely the result of disuse, as the same changes are seen if a limb is not actively utilized for any other reason. The "cold phase", which inevitably follows denervation, he attributes to a combination of postganglionic sympathectomy, subnormal metabolism in the part and no accumulation of the normal vasodilator metabolites. With regard to the etiology of the Raynaud phenomenon, no new explanations are offered, but the full discussion cannot fail to impress the reader how very unsatisfactory are the present concepts.

The book is attractively set out and well illustrated with photographs and diagrams and, with its comprehensive list of references at the end of each chapter, will prove informative, provocative and well worth reading by those with little or much experience in this field of medicine.

Donal M. Brooks

DENTAL SCIENCE

1242 An Atlas of Dental Histology

Edgar B. Manley & Edward B. Brain. Oxford, Blackwell Scientific Publications, 1947. xi + 49 pages; 22 figures; 102 plates. 25 × 19 cm. 12s. 6d. [£0.625]

(i) Enamel; (ii) dentine; (iii) cementum; (iv) pulp; (v) periodontal membrane; (vi) alveolar bone; (vii) development; (viii) absorption; (ix) enamel cuticle (Nasmyth's membrane); (x) epithelial root sheath of Hertwig; (xi) gingiva; (xii) histological technique; (xiii) ground sections; (xiv) decalcified sections; (xv) standing methods.

This book is dedicated to the memory of Dr. A. W. Wellings, and is intended as a guide for the student in his laboratory work. It is obvious, from even a casual glance, that an enormous amount of work has gone into the production of such a range of specimens and photomicrographs. Every part of the tooth and its attachments is copiously illustrated and on the whole the reproduction is excellent. A book of this type will be of value to students generally, but in particular to those who have access to the authors' lecture notes. To the research worker and advanced student, this book may be somewhat of a disappointment in that the descriptive matter is far too short and the reader is left with a series of unanswered questions. It is felt that the lettering of the photomicrographs could be improved, as the white discs obscure an appreciable amount of the part of the specimen to which they refer, and that more arrows could be employed to advantage. A truly excellent photomicrograph (Plate 47) is shown of Von Korff's fibres, and the following plates illustrating the nerves of the pulp deserve high praise. In the section on Nasmyth's membrane, Plate 88, depicting ends of the enamel prisms at a magnification of 55, leaves much to the student's imagination. One has also seen better photomicrographs than that of an enamel cuticle, Plate 89, depicting the ends of enamel prisms.

A section is included on histological technique to fulfil educational requirements of the General Medical Council, but it is felt that this could have been improved if the typical staining reactions of the various stains listed were given. Staining reactions do vary, but their inclusion would be of considerable help to the junior student. As pointed out by Professor H. F. Humphreys in the foreword, it must be remembered that the book is intended to supplement and not supplant the textbooks. Nevertheless, it is hoped that when a second edition is called for a further elaboration of its present scope will be contemplated.

E. Matthews

DERMATOLOGY

1243 A Practical Textbook of Leprosy

R. G. Cochrane. London, Geoffrey Cumberlege, Oxford University Press, 1947. xi + 283 pages; 174 figures; 1 plate. 25 × 19 cm. £2 2s. [£2.1]

(i) Introduction; (ii) etiology; (iii) epidemiology; (iv) pathology; (v) diagnostic and other serological tests; (vi) signs and symptoms; (vii) classification and technique of examination; (viii) atypical lesions and the development of esions; (ix) differential diagnosis; (x) reaction in leprosy; (xi) lesions of the nose, ear, mouth and throat: lesions of the eye; (xii) treatment of leprosy; (xiii) treatment of leprosy (*continued*); (xiv) treatment of leprosy (*continued*); (xv) treatment of neuritis in leprosy; (xvi) treatment of eye, nose and throat lesions; (xvii) treatment of trophic ulcers; (xviii) A. Treatment of syphilis in leprosy: B. Treatment of certain concomitant skin affections; (xix) A. Prognosis: B. Criteria of discharge and after-care; (xx) prevention of leprosy; (xxi) prevention of leprosy (*continued*): (xxii) practical methods of leprosy control. Appendices. Bibliography. Index.

As medical secretary to the British Empire Leprosy Relief Association and as Chief Medical Officer of the Lady Willingdon Leprosarium in Madras, the author has had a long and varied experience of leprosy. He has embodied that experience in the present work, which will be of interest to all leprologists. His reason for writing it is that he thinks that " . . . a practical textbook on leprosy would fill a gap between the type of book which deals largely with the theoretical aspects of the subject and the smaller pamphlets." In fact the text of his book is much longer, and unfortunately twice as expensive, as the standard english book on leprosy, by Rogers & Muir. It is somewhat uneven, for only two pages are devoted to the history of the disease and four to its etiology.

Epidemiology is rather more fully dealt with on modern lines, with emphasis on the low-age incidence, the great infectivity of the lepromatous type of the disease, and on the good prognosis of the tuberculoid form, the characters of which are illustrated in the pathological section by the author's photomicrographs. The prognostic value of the lepromin test and the want of any reliable serum diagnosis is brought out.

By far the best and fullest section is that containing well-illustrated clinical descriptions in which the important early symptoms are given special attention and the differential diagnosis of the different types of the disease is emphasized. The classification adopted by the Leonard Wood Memorial Conference on Leprosy (Cairo Conference, 1938) is used with some modifications. Atypical lesions are described in a separate chapter and are regarded as rare and intermediate between tuberculoid and lepromatous cases. Leprosy reactions are fully described and seven chapters are devoted to treatment, including that of the nose, throat and eye. The author relies on chaulmoogra preparations, but differs from most recent authorities in disparaging the use of sulphones, which have yielded such remarkable results in resistant lepromatous cases in the hands of Muir and of Louisiana workers.

The remaining chapters deal with preventive measures and are based mainly on the author's experience in Madras. Apart from some minor doubtful statements of an historical character, this section gives a good account of what is practicable under conditions in India; the importance of child leprosy, on which the author has written much, is stressed, as well as the segregation of infective cases, either in agricultural colonies, or if this is impossible because of lack of funds, in villages of their own. Because of the completeness of the clinical and treatment sections the work will be of practical value to leprologists everwhere.

1244 Atlas of Histopathology of the Skin

G. H. Percival, A. Murray Drennan & T. C. Dodds. Edinburgh, E. & S. Livingstone, Ltd., 1947. viii + 494 pages; 376 photomicrographs in colour. 24 x 20 cm. £3 15s. [£3.75]

(i) Terminology; (ii) normal histology; (iii) dystrophy and allied conditions; (iv) inflammation; (v) urticaria; (vi) lupus erythematosus; (vii) psoriasis; (viii) pityriasis rosea; (ix) lichen ruber; (x) pityriasis rubra pilaris; (xi) eczema; (xii) cheiropompholyx; (xiii) primary vesiculobullous eruptions of internal toxic origin; (xiv) primary vesiculo-bullous eruptions of external origin; (xv) pustular eruptions; (xvi) tinea; (xvii) rosacea and rhinophyma; (xviii) granuloma pyogenicum; (xix) traumatic injuries and the effects of stress; (xx) the reticuloses; (xxi) granulomatous conditions; (xxii) the naevi; (xxiii) cysts; (xxiv) tumours. Index.

The first reaction on turning over the pages of this new book is that the text is exceedingly brief for one so richly illustrated with coloured reproductions. However, on reading the preface one finds that the authors have, very fairly, already advised the student—and the reviewer—that the book purports to be an atlas and not a textbook of histopathology of the skin, and that their objective is " to portray in pictorial form the microscopical changes found in the more common diseases of the skin ", the text being " severely limited just to what seemed necessary to explain briefly the processes illustrated ".

The authors have certainly adhered rigidly to their intention in the greater part of the book. Exclusive of the descriptive notes beneath the illustrations, the text devoted to the subjects covered in the first 100 pages is written in about 450 lines, of which 52 are given to the Introduction, 50 to Terminology and 20 to Normal Histology, the remaining 325 being spared for the descriptions of " Dystrophy and allied conditions ", " Inflammation ", " Urticaria ", " Lupus erythematosus ", " Psoriasis ", " Pityriasis rosea ", " Lichen ruber " and " Pityriasis rubra pilaris ". On reflection one cannot help but think that this is far too austere a use of words, particularly when the authors consider that the subject " Eczema " merits the relatively extravagant use of 320 lines.

The study of pathology of the skin is, like that of other diseases, by no means so simple that one can acquire sufficient knowledge by illustrations alone, and brief descriptions may not only be of little use but also prove very misleading. Of these there are many examples in the book, of which one may cite: " Sarcoid—the histological picture in the various clinical types of sarcoid is essentially that of a tuberculous process. The infiltration is circumscribed, it is deeply situated in the dermis and caseation is absent." Except for the last feature, most would disagree, for surely the picture differs considerably from the typical tuberculous reaction and " the infiltration ", whatever that term denotes, is not usually situated deeply in the corium.

It is frequently argued that photomicrographs give a more accurate portrayal of a section than a drawing, an opinion with which the reviewer does not concur, for no matter how critical is the focusing, one must of necessity incorporate in the picture much that is above and below the plane of focus and which must therefore appear blurred, a factor which one eliminates on visual microscopical examination by frequent use of the fine-adjustment screw. It is for this reason that illustrations of cellular changes in the corium, as for example those found in chronic granuloma, prove of little value.

If only the authors could be persuaded to give rein to their extensive and valuable knowledge of the subject by enlarging the text and improving some of the deficiencies of illustration, the literature of this subject would indeed be considerably enriched.

1245 Skin Manifestations of Internal Disorders (Dermadromes)

Kurt Wiener. London, Henry Kimpton, 1947. 690 pages; 386 text-illustrations; 6 colour plates. 25 × 18 cm. £3 3s. [£3.15]

(i) The dermadromes of systemic infections; (ii-viii) systemic infections; (ix) helminthic diseases; (x) tuberculosis; (xi) dermatoses with claimed but still controversial tuberculous etiology; (xii) leprosy; (xiii) dermadromes of intoxications; (xiv) disorders of the circulation; (xv) diseases of the kidneys; (xvi-xx) disorders of the endocrine glands; (xxi) puberty; (xxii) menstruation; (xxiii) pregnancy; (xxiv) childbirth and puerperium. The skin in the newborn; (xxv) menopause; (xxvi) miscellaneous dermatoses with endocrine background; (xxvii) ageing; (xxviii-xxxi) metabolic disorders; (xxxii-xxxiv) disorders of the blood and blood forming organs; (xxxv) dermadromes of internal cancer; (xxxvi-xxxix) disorders of the nervous system; (xl) psychoses and psychodermatoses; (xli) disorders of the gastrointestinal tract; (xlii) diseases of the liver and pancreas; (xliii) disorders of the respiratory tract. Index.

A considerable proportion of the medical books published cover almost the same ground as others which are in current use. It is a refreshing change to find a book which deals with an unhackneyed aspect of medicine. The subject is treated broadly and in detail and all borderland topics are included.

The first 12 chapters are devoted to systemic infections and infestations. They include an account of the acute specific fevers with detailed descriptions of their exanthematous manifestations. Much of this material comes within the realm of a physician

rather than a dermatologist. The section entitled Dermatoses with Claimed but still Controversial Tuberculous Etiology contains a strange mixture: erythema nodosum, granuloma annulare, sarcoid, lupus erythematosus, and others. The etiology of these various disorders is discussed fairly.

Dermatitis medicamentosa is then discussed fully and includes an account of "atypical lichen planus" due to mepacrine (atabrine). This is followed by disorders of the circulation and of the kidneys. One of the illustrations suggests a confusion between Schamberg's disease and stasis dermatosis.

The most interesting part of the book is contained in the 15 chapters on endocrine and metabolic disorders. A brief description of each disorder is followed by a full account of its "dermadromes." The author's judgement seems to be faulty in suggesting estimations of the basal metabolic rate in all cases of vitiligo because this condition occurs in 10% of cases of thyrotoxicosis. A long list of dermatoses is given in which evidence has been produced for relationship to ovarian dysfunction, especially in individual cases, but the wise statement is made that "no dermatosis has been described which by its morphological picture alone would invariably permit the diagnosis of an ovarian dysfunction or disease." The section on puberty contains a particularly good and fair discussion of the part played by the gonads in acne vulgaris. The account of the dermatoses connected with menstruation, pregnancy, the puerperium, and the menopause abounds with information which is of great importance and which is by no means widely known. Under the heading "diabetes" Urbach's work on skin sugar and on "cutaneous glycohistechia" ("dermal" would have been better) is described. The account of the vitamin deficiencies is orthodox. Among the conditions for which treatment with vitamin D may be given, lupus vulgaris is not mentioned.

The chapter on ageing includes a chronological account of the onset of wrinkles in the various areas of the skin. It is stated that the first wrinkles appear on the forehead and lower lids at the age of twenty-five.

As in all american works, the reticuloses are called "lymphoblastomas". The skin manifestations of leukaemia are divided into specific and non-specific. Following the chapters on the blood there are accounts of skin in internal cancer and in disorders of the nervous system.

The chapter entitled Psychoses and Psychodermatoses is the weakest in the book. It is interesting as far as it goes but it is quite inadequate. The surprising statements, "Purely psychogenic *urticaria* is rare" and "purely psychogenic pruritus is rare", give a clue to the author's scepticism of the importance of psychogenic factors except as trigger mechanisms.

The final chapters deal with digestive and respiratory disorders. They are followed by seven tables, the first of which summarizes much useful information about the acute exanthemata. The second deals with diffuse pigmentations, the third with diffuse yellow pigmentations, the fourth with hypertrichosis, the fifth (an excellent and unusual presentation) with the skin in relation to age, the sixth with haemorrhagic diseases, and the last with pruritus. These tables are carefully compiled and make a valuable addition to the book. Unfortunately psychotherapy is not specifically mentioned in the list of ten treatments for pruritus. The index occupies 14½ pages, but could profitably be extended.

This is a very valuable reference book for dermatologists and probably also for the general physician. There are 3110 references, a considerable proportion of which pertain to the german literature. These references, in which there are a few misprints, are in the form of footnotes; at least one of the small numbers in the text is misplaced. The method of setting out the references seems to follow no system; in most of them the year follows the volume and page number, but in some it precedes them; in some the title of the paper is given in its original language and in some it is translated into English. There are a few surprising omissions, e.g., the books by Broster and his colleagues in the section on adrenal tumours, by Stannus on avitaminosis A, and Kuno in the section on sweating (though reference is made elsewhere to his work). Most of the 386 black-and-white illustrations are excellent but a few (e.g., fig. 17) are poor; some of the coloured plates are valueless. An immense amount of work has gone into the writing of this book and the publishers have produced it admirably.

E. Lipman Cohen

ENDOCRINOLOGY

1246 Endocrine Function of the Hypophysis

Harry B. Friedgood. New York, Oxford University Press; London, Geoffrey Cumberlege, 1946. iv + 240 pages; 36 figures. 24 × 16 cm. £1 5s. [£1.25]

This book is reprinted from the Oxford Loose-Leaf Medicine and its presentation stands quite well alone, although it is not comprehensive. The first half of the book, on embryology and physiology, is not as good as the clinical sections, although great pains have been taken to give detailed references for many of the statements.

There is a slight confusion in the references to the cytology of the pars anterior (Tilney, 1938; Bucy, 1932) and the statement that the "cortical zone consists essentially of basophile cells" is quite contrary to the findings in man or to the original extraction of growth hormone from the bovine cortical rim of the anterior pituitary of cattle with its high eosinophil content. Of man, A. T. Rasmussen states quite clearly[1], and it is also the experience of the pathological department of the London Hospital, that:

> Histologically even more unreliability existed because of the habit of diagnosing the entire gland by general inspection of a single section, which too frequently was near the mid-sagittal plane. In the human hypophysis the distribution of the different types of cells is so irregular that nothing short of several horizontal sections suffice.
>
> The acidophils tend to concentrate in a large area located somewhat posterially in each lateral half of the anterior lobe, leaving an area near the mid-sagittal plane and an anterior and a marginal zone where the acidophils are less numerous and hence richer in chromophobes and basophils.

A good deal of evidence is produced in favour of the basophil-cell origin of follicle-stimulating gonadotrophins, but it is also pointed out that luteinizing hormone is secreted by acidophil cells, which is not generally appreciated. The pathological physiology of exophthalmos is well dealt with and the long pages of closely printed matter are happily relieved in this section by excellent illustrations. The section on the complicated physiology and pathology of growth is excellent, with a very full bibliography. This section is followed by a sound clinical one on giantism and acromegaly. The statement that "the growth of the hair on the head is remarkably thick" might be more qualified and is certainly not true of women, in whom it often falls out, as in primary virilism. The polyuria of acromegaly is well described but no reference is made to the opposite condition of diabetes tenuifluus, due to excessive secretion of pitressin, which may be present in some phases of acromegaly and is then associated with oliguria and excessive perspiration.

Attention is drawn to the fact that the epiphyses of giants "remain ununited many years beyond the period of normal ossification." This fact, not generally appreciated or known, does not refer to the tall eunuchoids, but to giantism associated with an eosinophil adenoma or hyperplasia and must be ascribed (although this is not stated in the book) to the fact that hypogonadism is an accompaniment of the disorder. The statement is by no means true of all giants, and closure of the epiphyses may even be relatively premature, the great height being due to excessive secretion of growth hormone in childhood and early adolescence.

In summary, this is a good book, with full information on many aspects of a very involved subject, and deserves a place in the library of every scientific endocrinologist.

S. L. Simpson

[1] *The pituitary gland* (Proceedings of the Association for Research in Nervous and Mental Disease, December 1936), Baltimore, 1938.

1247 The Glands of Destiny: a Study of the Personality

Ivo Geikie-Cobb. Third Edition. London, William Heinemann Medical Books, Ltd., 1947. xii + 258 pages; illustrations. 22 × 14 cm. 15s. [£0.75]

Part I. (i) Introduction; (ii) the ductless glands and their secretions; (iii) the thyroid gland; (iv) the parathyroid glands; (v) the pituitary gland; (vi) the adrenal glands; (vii) the sexual secretions of the male; (viii) the female sex glands and their secretions; (ix) the internal secretions of digestion; (x) the pineal gland; (xi) the thymus gland; (xii) the internal secretions and the nervous system. Part II. (i) Personality and the internal secretions; (ii) the internal secretions in everyday life; (iii) racial characteristics and endocrine influences; (iv) from infancy to old age; (v) civilisation and warfare; (vi) on giants; (vii) on dwarfs; (viii) the present position of organotherapy; (ix) personalities; (x) the summing-up. Epilogue. Glossary. Bibliography. Index.

The sub-title of this book is " A Study of the Personality " and in this field it achieves a measure of success and historical interest. It is quite obvious that the writer is a man of culture and historical knowledge and a keen and thoughtful observer. Nevertheless the attempt to link his observations on personality with modern endocrinology, or even ancient endocrinology, is very weak and very often completely beyond any known facts. There is also a good deal of muddled and erroneous conjecture.

Of Henry VIII we read that " the anterior pituitary was probably somewhat countered by the posterior, otherwise the artistic element would not have been so marked "; of Queen Elizabeth, " the needs of a queen had called forth those glands which help to fight and to govern "; of James I, " his features and character point to a post-pituitary-thyroid dominant type "; of Charles I, " a little less of the posterior-pituitary and a stronger, better balanced, more masculine man might have resulted." All this may be very intriguing to the lay reader but to a scientific endocrinologist it is largely nonsense. This does not mean that the endocrine glands do not contribute to personality or that diseases of them may not seriously affect personality. A scientific treatise on this subject is yet awaited and maybe it is better to wait another decade before attempting it.

In the first section of the book, dealing with the function of the separate endocrine glands, there are innumerable mistakes. Thus a mongol, " like a cretin ", is said to have " a puffy mis-shapen body with dry skin, subnormal temperature and slow pulse ". Parathyroid deficiency is attributed to alimentary poisoning and the obsolete guanidine theory resuscitated. Pituitary feeding by mouth for obesity is advocated, whereas all scientific evidence fails to substantiate any such claims. " Anyone who can fall asleep at will would probably benefit from a stimulant to the pituitary gland." " Hypofunction of the adrenal medulla may exist as a disease entity, hypoadrenia." " The logical opposites of acromegalics are the short swarthy goat-legged achondroplasics."

Although nothing can really compensate for such errors in a book dealing with endocrines there are interesting historical chapters on giants and dwarfs with case-histories and quotations. On the subject of glands and personality, the author unfortunately quotes from another book which has no greater scientific basis for many of its statements than his own. If the preface made clear that the book was for lay readers and that it had no scientific pretensions, it would serve the purpose of amusing and interesting without doing any great harm.

S. L. Simpson

GERONTOLOGY

1248 Old Age: its Compensations and Rewards

A. L. Vischer. London, George Allen and Unwin Ltd., 1947. 200 pages; 9 illustrations. 22 x 14 cm. 12s. 6d. [£0.625]

(i) Senescence as a bodily and mental process; (ii) the duration of life; (iii) society and the individual: their attitude toward old age. Bibliography.

This book is an essay on the psychological and social aspects of old age written by one well qualified to do so in virtue of his twenty years' experience as physician to the Old People's Home of the city of Basle. The author is essentially a humanist, as is frequently displayed in his treatment of the physiological and pathological problems of senescence. His description of the gross changes in old age is excellent, but his explanations of them are such as must be regarded as unsatisfactory both by the scientist and the philosopher. Such statements as " life is gradual dying " and " ageing is a conflict between the nobler elements . . . and the simpler elements ", though possessing attractions as artistic symbolisms, must remain unhelpful half truths.

Vischer shares the views of Bastai and Dogliotti that the actual cause of old age is an insoluble problem which is best left to the philosopher. It is to be hoped that the scientist of today approaching this problem of great interest and even greater social importance will not accept such an attitude.

In the second part of the book the author is dealing with matters of which he has very great knowledge. His main theme is that with successful adaptation of the individual and of society old age can be and often has been a phase of achievement which in its own way need not be inferior to or less happy than youth. His failure to draw a sharp line between mere chronological age and physiological age weakens his position. He makes great play of the fact that a great painter given fifty years to develop his art may in the end produce finer pictures than in the beginning. This, of course, is a verifiable fact, but it does not dispose of the difficulty that a great many artists must have been prevented from their own further evolution by such conditions as cataract or paralysis agitans. Vischer's ideas concerning the compensations and rewards of old age presuppose as a minimum condition the preservation of the central nervous function. He forgets, however, that Montaigne said " en ay assez veu, qui ont eu la cervelle affoiblie avant l'estomach et les jambes ".

This book has many merits. Where the author is calling upon his own experience concerning the care of old people, the nature of their needs and of the means of finding a place for them in society, he writes with great knowledge and understanding. In the latter half of the book, where he is reviewing the position of the aged in society throughout the centuries and the achievements of old people, he provides a veritable anthology of the best that both the past and present have to offer. His main contention that old age can and should be a stage of fulfilment rather than of frustration is well sustained by many examples from history and by the inclusion of some interesting reproductions which contrast the early and the late work of such masters as Titian, Tintoretto, Bernini and Renoir.

There must be but few who are interested in the problems of gerontology and geriatrics by whom this book will not be found both interesting and helpful.

F. A. E. Crew

HEALTH THROUGH EXERCISE

1249 Physical Education

E. Harold Le Maistre. Melbourne, Oxford University Press; London, Humphrey Milford, 1945. xv + 310 pages; 67 figures. 22 x 14 cm. 11s. 6d. [£0.575]

(i) The history of physical education; (ii) the aim, objectives and principles of physical education; (iii) the scope and nature of physical education; (iv) safety in physical education; (v) the hygiene of physical education programmes; (vi) the relative value of physical education activities; (vii) anatomy and physiology; (viii) muscle location and action; (ix) tests and measurements in physical education; (x) posture; (xi) exercise and fatigue; (xii) tournaments and draws; (xiii) court, field and equipment specifications; (xiv) future trends in physical education. Selected bibliography for detailed references. Index.

This is a small compendium which is designed, in the words of the preface by Professor Harvey Sutton, " to bring before the teacher the scientific basis of the work, to set out a synopsis of our knowledge of structure and function of the human body, and also to furnish a wide variety of techniques for various sports and games in Australia." It thus deals with a wide variety of subjects ranging from a somewhat bare account of muscular attachments and actions, the physical activities of aboriginal Australians, the principles on which games shall be organized, physical tests and measurements and statistical methods, to the specifications for fields, courts and equipment, and a few data regarding gaseous exchanges in the body.

All topics are necessarily dealt with in a very abbreviated form, but as a work of reference it should be useful for the more administrative aspects of physical education. So far as the scientific aspects of human anatomy and physiology are concerned the very brevity of this book and the selection of its contents will tend to give teachers a superficial approach to a real understanding of the working of the body, and might indeed encourage the " cramming " of students, leaving their minds clogged with details of which they cannot appreciate the significance. It seems useless to enumerate the varieties of neuroglia, while the references to pH of the blood and to blood-buffers may convey a false sense of understanding unless the reader re-reads the elements of physiological chemistry elsewhere. The brief statements made regarding reflexes assist little in an understanding of their significance for physical education. Even the accounts of muscular actions are singularly incomplete; in the analysis of fundamental actions, the arm alone is dealt with. Nor is there any attempt at the analysis of the movements involved in exercises or games.

Mr. Le Maistre's book can be recommended as a convenient reference work in regard to simple details for those whose knowledge is already much wider than that presented by this book.

MEDICAL HISTORY

1250 Magic and Healing

C. J. S. Thompson. London, Rider & Company [1947]. 176 pages ; 20 illustrations. 22 × 14 cm. 15s. [£0.75]

(i) Magic and healing—early beliefs in the origin of disease; (ii) healing by incantation; (iii) healing and astrology; (iv) transplantation of disease; (v) healing by sympathy; (vi) healing by touch; (vii) healing in ancient Britain; (viii) Anglo-Saxon herb-lore and wort-cunning; (ix) the healing art in ancient Wales; (x) the healing art in ancient Eire; (xi) folk-medicine in Britain; (xii) the doctrine of signatures and its influence on healing; (xiii) traditionary herbs of healing; (xiv) plants of the devil; (xv) herbs and plants dedicated to saints; (xvi) plants and drugs used by sorcerers; (xvii) remedies of animal origin employed by the Anglo-Saxons; (xviii) precious and rare stones employed in healing; (xix) man's body and its use in healing; (xx) magical girdles used in healing; (xxi) magical and medicinal rings of healing; (xxii) magical stones of healing; (xxiii) horns of healing; (xxiv) miraculous beds of healing; (xxv) colours and numbers and their influence on healing; (xxvi) toothache and its cure in antiquity; (xxvii) the psychological effect of magic in healing.

The author of this book, Dr. C. J. S. Thompson, who died in 1942, was an acknowledged authority on primitive medicine and on the art of the alchemist and the apothecary. That he loved to probe the mystery surrounding those subjects is evident from the fact that the word " Mystery " is included in the title of twelve of his previous works—The Mystery of Poison, of Pharmacy, of Perfume, or of Astrology and of Apparitions alike intrigued him and guided his pen to produce those fascinating and interesting studies.

The present posthumous work was left unfinished by the author, but it has been prepared for the press by his son and daughter, who are to be congratulated on the successful accomplishment of a difficult task. The only criticism, which many readers will share with the reviewer, is that this little work is overweighted with information, so that each page demands a serious study which rather detracts from the enjoyment of the reading. This difficulty is immensely increased by the absence of an index. For a work of this nature, an index is essential, and it is hoped that this defect may be remedied in future editions. The material is classified in 27 chapters. From Early Beliefs regarding Disease, we pass to Healing by Incantation and by Touch, to Plants of the Devil and Plants of the Saints, to Magical Girdles, Medicinal Rings, and Miraculous Beds, the Doctrine of Signatures, and the Influence of Colours and Numbers. The subject of medical folklore is immense, but its literature is relatively scanty. This new work is therefore to be accorded a welcome, a welcome somewhat saddened by the reflection that it is Dr. Thompson's last book. The illustrations are unusual and well chosen, but one misses a bibliography almost as much as an index.

Douglas Guthrie

1251 Joseph Lister : Father of Modern Surgery

Rhoda Truax. London, George G. Harrap & Co., Ltd., 1947. 270 pages ; 10 illustrations. 20 × 14 cm. 10s. 6d. [£0.525]

(i) The godless college; (ii) bachelor of medicine; (iii) the formidable; (iv) the killer in Glasgow; (v) the tragic Hungarian; (vi) living ferments; (vii) the killer revealed; (viii) test cases; (ix) presenting the evidence; (x) the discredited ligature; (xi) professor of surgery; (xii) innovations; (xiii) the vivisection controversy; (xiv) bitter opposition; (xv) the decision; (xvi) the centre of resistance; (xvii) storming the citadel; (xviii) the turning-point; (xix) antisepsis and asepsis; (xx) the long honeymoon; (xxi) Joseph, Baron Lister; (xxii) another Herakles.

This can scarcely be regarded as a new book. It is, indeed, the british edition of a biography which was first published in the USA several years ago. Nevertheless, as Lord Horder remarks in his illuminating foreword, " . . . we may surely welcome an edition of Rhoda Truax's biography of Joseph Lister in the country that boasts his birth and his life's work."

One may find it hard to realize that Lord Lister died as recently as 1912, and that only 82 years have passed since he first introduced the antiseptic method which was destined so soon to revolutionize the whole practice of surgery. The story of Lister's early life and training, of his adaptation of Pasteur's discovery of what was called " the germ theory " to the needs of surgery, of his struggle for the acceptance of his views, and of his ultimate complete success—all form a fascinating story and a noble theme for the biographer. Although there have been several biographies of Lister since the first authoritative work by his nephew Sir Richman Godlee appeared in 1917, there is still room and demand for a short popular account, designed for the non-medical as well as for the medical reader. The work under discussion is a treatise of this nature, following conventional lines and portraying the old familiar facts, accurately and attractively, and all within the compass of 270 pages. It is a most interesting and readable description of the achievement of one of the greatest figures in the long history of medicine, who, by his introduction of the antiseptic method, earned so well the title of Father of Modern Surgery. The illustrations, rather poor, and bunched together in the second chapter, are a disappointing feature of the book, and there is a tendency to dramatize the facts and to introduce imaginary conversations to an extent less favoured on this side of the Atlantic than in America. There is, however, a useful index and a bibliography.

Douglas Guthrie

MEDICINE AND LIFE

1252 The Occasion Fleeting

Hugh Barber. London, H. K. Lewis & Co. Ltd., 1947. viii + 199 pages. 22 x 14 cm. 15s. [£0.75]

(i) The pre-clinical years; (ii) the clinical years in a medical school; (iii) the provincial hospital years; (iv) medicine and morbid anatomy; (v) clinicial acumen; (vi) the history and the signs; (vii) the consultant and the specialist; (viii) the spirit of the family doctor; (ix) the relatives and friends; (x) the art of the geriatrician; (xi) psychosomatic medicine; (xii) medical examination in the absence of symptoms; (xiii) the beginnings of disease; (xiv) medicinal remedies; (xv) pathognomy at the bedside; (xvi) doctors' dilemmas; (xvii) alcohol in its place. Bibliography.

This is a collection of essays, largely reminiscential in character, embodying the clinical wisdom acquired by the author during a long medical career of nearly half a century. The title will be known to all medical men, perhaps not to so many laymen, who may also read the book with pleasure and profit. It is a quotation from the first aphorism of Hippocrates, ὁ δὲ καιρὸς ὀξύς, and sets the tone for the whole work, which abounds in aphorisms, some original, many quoted. As examples of the former we may cite: " in diagnosis and treatment he gets the best results who has a receptive countenance "; " one generation is looking for a sign which may be discredited by the next, but clinical histories have a way of repeating themselves and live "; " right character, developed in childhood, is the best insurance against avoidable disease "; " examination passing is partly a necessary evil and partly good fun ". Some of these aphorisms occur more than once in different essays, but criticism on this score is disarmed by a quotation from *The autocrat of the breakfast-table :* " He must be a poor creature that does not often repeat himself ". Oliver Wendell Holmes, to judge by the frequency with which he is quoted, must be one of Dr. Barber's favourite authors: others are Laurence Sterne, Samuel Johnson, Robert Louis Stevenson, Lewis Carroll, Rudyard Kipling, and among medical writers Sir William Withey Gull, Sir William Osler, Sir James Mackenzie and Wilfred Trotter. Inserted between the essays are short fables designed to point the moral of what has gone before. Like most attempts of this kind they are apt to be somewhat dull, and thus fail to achieve their purpose.

Dr. Barber has a wealth of anecdotes, which are indeed one of the most attractive elements in his book, but his concluding remark, " one could write an essay on that ", palls through too constant repetition. We like particularly the story of the country practitioner who was thrown into a ditch from his motor bicycle and knocked unconscious. On coming to, he found a ring of people standing over him and heard a voice saying, " Well, there now, if it isn't our own dear Doctor, and we've sent for him to come and see hisself ". There is also the slightly " naughty " one about the young married woman who wished her doctor to attend at her confinement, but was emphatic that she could not ask him to call to fix up the date, because it was his invariable custom on entering the room to say, " Well ! What have you been doing ? "

If one can attempt to catch any general theme running through the various essays of this book it is a somewhat wistful eulogy of the old-fashioned " family doctor ", a term that Dr. Barber prefers to general practitioner. While recognizing and acknowledging the advantages brought by recent advances in medical science, he repeatedly expresses the view that we have lost something too in the passing of the older methods and customs. One

gathers, as much by reading between the lines as from any direct statements, that Dr. Barber views with some apprehension the advent of a national health service. In the following passage he even allows a note of cynicism to creep in which is foreign to the general tone of the book: "There will be less room for individual worldly wisdom in a new world which may believe itself to be wise; although it may behove a young man to touch his cap to a superior officer". Nevertheless the evils of the financial basis of private practice are exposed in several passages; for instance, " . . . it would have been rather nice to have refused to price a particular service; and this is one of the privileges of the honorary staff to a hospital"; or again, " . . . it is probable that there is no other calling in which the conflict between the scientific side and the financial side is so acute as it is in medicine". An example of how financial considerations may complicate practice is given in the chapter on the art of the geriatrician: " a young doctor's first idea should be as to whether he can earn the money; by which I mean deserve it". In another connexion however the profit-motive is upheld: "In British medicine, of which we are justly proud, the consultant has relied economically upon the support of the family doctor. It has been an excellent stimulus." Moreover, in one of the longest passages of the book devoted to a single topic, Dr. Barber defends in no uncertain terms the buying and selling of practices, concluding with the triumphant parting shot: "If the new service shows shortcomings in some directions, as well it may, I only wish to state that it must not be claimed as a set-off, that the public have been saved from the indignity of being bought and sold like chattels, because for those members of the community whom it concerned the results were excellent".

One of Dr. Barber's chief interests apart from medicine is obviously cricket, for metaphors and analogies from the game occur constantly throughout his book, and he proudly claims the most distinguished player as a member of his own profession. There stand out from these pages not only a charm and urbanity of manner but also a kindly, tolerant spirit that we believe it is not altogether fanciful to attribute to Quaker influence : the author's grandfather was a Quaker and he himself was at a Quaker hall of residence while a student at Manchester. The quotation from William Penn's *Fruits of solitude*, at the head of the essay on the consultant and specialist, is also significant.

We can imagine no more appropriate gift for a retired "family doctor" or layman with a "medical background" than *The occasion fleeting*, and we hope the author will not take it amiss if we describe it as an ideal bedside book. If we have read his character aright, he will not do so.

Cyril C. Barnard

1253 The Doctor's Job

Carl Binger. London, George Allen & Unwin Ltd., 1947. 243 pages. 22 x 14 cm. 12s. 6d. [£0.625]

(i) Background and changes; (ii) specialities and specialists; (iii) the choice of physician, medical fees and etiquette; (iv) the relationship of doctor and patient; (v) medicine and psychoanalysis; (vi) psychiatry and medicine; (vii) some common psychiatric problems; (viii) psychosomatic medicine or mind and body relationships; (ix) stomach ulcer; (x) allergy, asthma and tuberculosis; (xi) high blood pressure; (xii) the cure and control of disease; (xiii) recent achievements and tasks ahead; (xiv) convalescence and chronic disease; (xv) the prevention of illness; (xvi) office practice, hospitals and outpatient departments; (xvii) socialized medicine or paying the piper; (xviii) past, present and future. Bibliography. Index.

It is a pleasure to review a book like this, written evidently by a man who has put into it not only his great learning and experience, but his heart. This is clearly shown by the conclusion announced by the author in his introduction: "Nothing a man has of scientific acumen, personal integrity and human understanding is too much to bring to this job." In one reader at least the book created not only an increased pride in his profession but a lingering doubt whether anyone but a superman is equal to this task.

Dr. Binger deals with every aspect of medical work and always with emphasis on its effects on the mind and body of the patient, who is continually in the picture. He shows what a complicated and costly business the prevention, diagnosis and treatment of disease have become. In spite of sympathetic references, the author comes to the conclusion that in a modern industrialized world the day of the general practitioner is past. His place is to be taken eventually by the trained internist working mainly in a hospital or centre with co-operation whenever necessary with the specialists. The number of these in the USA is indeed formidable—no less than 26 varieties officially recognized. Dr. Binger has some very wise remarks on their limitations as well as their virtues, and on the best ways of using them.

A particularly noticeable feature of the book is its insistence on the interaction of mind and body. Dr. Binger says, "The approximation of psychology and medicine is one of the most important steps, as yet perhaps not fully appreciated, which modern medicine has taken." His chapter on the psychiatrist, while cleverly dispelling some of the "mystery-man" atmosphere which has grown around him, is absorbing and to me convincing. Another of Dr. Binger's dicta is almost a summary of his intention in writing this book: "It is almost as important to know what kind of a patient has the disease as what kind of disease the patient has."

Tempting as it is to dwell on each chapter of the book I must resist it and come to the section which deals with the crucial question of how this complicated and expensive modern medicine can be brought within the reach of the ordinary citizen—a problem which is exercising the minds of politicians as well as doctors all over the world. Dr. Binger points out that even in the USA, the world exemplar of private initiative and voluntary effort, the socialization of medicine is making great strides. "At least three-quarters of the total number of hospital beds in the United States are paid for out of public funds," he states, and he evidently believes that this tendency will extend to other forms of practice. He speaks very sympathetically of the many interesting experiments in voluntary prepaid medical insurance and group practice but regards them as merely touching the fringe of the problem. A criticism I must offer on this part of the book is that Dr. Binger does not seem sufficiently to appreciate the potential dangers to the best traditions of our profession, and to the public, if and when the State becomes the chief paymaster, instead of the patient.

This fine book is one that every doctor and medical student would profit by, and it can be just as cordially recommended to the intelligent layman, for the thought and hard work that have gone to its making are concealed by the ease and lucidity of its style.

Alfred Cox

1254 János, the Story of a Doctor

John Plesch. London, Victor Gollancz Ltd., 1947. 579 pages ; 37 illustrations. 20 × 13 cm. 18s. [£0.9]

Part I. Science, politics and personalities. Part II. The theatre, art, music and England. Appendix: a doctor's dialogues. Index.

Although the subtitle of this book is The Story of a Doctor, it seems more important that it is the story of a highly intelligent and versatile man: his life, his opinions and his anecdotes. As the first has been exceptionally rich and varied, the second are sound and freshly stated, and the last are harvested from intimacy with many of the great ones of Europe (among them Einstein, Kreisler, Reinhardt), it is full of interest.

Like too many autobiographies it is almost formless, resembling a life-time notebook arranged loosely into sections and into some chronological order. The writing is diffuse and without style, although this no doubt is partly because the book, as we have it, is a translation—from what language, curiously enough, the publishers do not tell us. It would be hard even to guess the language of the original, since according to the author's own account he has at different periods of his life used Turkish, Hungarian, German, Slovakian and "quite a smattering of Roumanian." It is hardly necessary to say that Dr. Plesch grew up in the polyglot, patriarchal atmosphere of the Austro-Hungarian Monarchy, where he learnt not only his languages, but acquired an early love for the arts, particularly music, and for medicine. "I grew up amongst doctors," he writes, "and from my earliest childhood I never had any other idea but to become a doctor myself." Yet for some time he seems to have faltered in his choice of profession, until the unnerving privilege of once conducting the crack band (usual conductor one Franz Lehár) of the austro-hungarian army, after which he finally renounced music in favour of medicine. Because the terms in hungarian universities started and ended at different times from those in the rest of Europe, during the long summer vacations he was able to go to the great medical centres of Austria, Germany and Italy—"to any place where some great man was at work whose reputation attracted me."

He was in Berlin five years before Virchow's death, made his acquaintance and watched him dissect. After Hitler's rise to power Plesch, with his wife and three children, came to England, where he requalified and settled.

The author's own character and versatility, as well as his exceptional opportunities, must have helped to form the extraordinary galaxy of friendships of which the anecdotes adorn this book. The multitude of accounts of the notable or notorious of Europe between the two world wars is almost bewildering and it is often difficult to disentangle authentic personal experience from hearsay.

In the search to discover a satisfactory explanation of the purpose of life, Dr. Plesch accepts Goethe's motto, " that the practical solution is that life is there to be lived." He employed this motto not only in his advice to some of his patients, but lived up to it fully himself. It is a pity that occasionally his words (or those of the translator?) give the impression that the author is too conscious of his achievements, which left the reviewer sometimes with an embarrassed sensation. One tends, however, to forgive such slight indiscretions from a man who is not only knowledgeable in his profession but also a connoisseur of the values of civilized life. Apart from music, in which he showed talent in early youth, one of the illustrations in the book, a portrait of Einstein by the author, bears witness—to say the least—that he could paint, and he also had wide knowledge of the european stage, its actors and producers.

But not the least interesting are the author's opinions. Here he is often unorthodox, sometimes provocative, but never stupid. He advocates euthanasia, legalized abortion and tolerance of homosexuality. He says many wise and often original things about marriage, sex and about the doctor-patient relationship. He believes in moderation not only in the natural good things of life, but also in sport and in fresh air—a refreshing conception!

By opening the book at the index first, the reader may get a very good idea of the number of subjects treated—indeed, the author shows some immoderation in inclusion of subjects—but on all of them he displays humanism, humour, and open-minded intelligence.

G. Popjdk

MICROSCOPY

1255 The Microscope and the Practical Principles of Observation

Theodore Stephanides. London, Faber & Faber Ltd., 1947. 160 pages ; 20 illustrations. 22 × 14 cm. 10s. 6d. [£0.525]

Part I. Description of the microscope. (i) the stand; (ii) the optical system; (iii) choice of a microscope. Part II. Technique of microscopical observation. (iv) Illumination by transmitted light; (v) illumination by diffracted light or dark-ground illumination; (vi) binocular microscopes; (vii) methods for recording observations. Bibliography. Appendix. Index.

It is a curious fact that, perhaps more than any other instrument, the microscope has attracted the attention of those who in the best sense of the word are " amateurs ". Such amateurs as Joseph Lister, Nelson and Barnard have made most important additions to microscopy. It is therefore not surprising to find that the writer of a book on the microscope is a greek poet, who happens also to be a medical man.

Many books on microscopy describe fully the preparation and staining of animal and plant tissues and other objects for microscopical study but give little or no instruction as to their examination when actually upon the stage of the microscope. The present volume attempts to meet this want by giving a methodical survey of the technique of microscopical observation. Although it is written primarily from the medical angle the fundamental principles remain the same for all branches of microscopy. The first part of the book gives a systematic description of the microscope, with instructions on the choice of an instrument for particular purposes. Especially important is the insistence on a microscope with the standard Royal Microscopical Society's eyepiece, objective and substage diameters. The second part of the book deals with the technique of microscopical observation and here even those who are expert microscopists may discover points of interest, though they will by no means agree with every statement made. The causes of errors of interpretation due to bad centring of the optical system, bad focusing of the condenser, bad regulation of the illuminating cone and bad correction for spherical aberration are well described. Information, not always easy to find in works on microscopy, is given on simple methods for determining the dimensions of an object, its shape and position. A bibliography of books giving more information on particular questions and an appendix with definitions of terms used in microscopy complete a useful if elementary book, which incidentally is written in impeccable English.

G. M. Findlay

NERVOUS SYSTEM

1256 The Physical Background of Perception: Being The Waynflete Lectures Delivered in the College of St. Mary Magdalen, Oxford, in Hilary Term, 1946

E. D. Adrian. Oxford, Clarendon Press, 1947. 95 pages ; 21 figures. 22 x 14 cm. 10s. [£0.5]

(i) The brain and the mind; (ii) the sense organs; (iii) motor and sensory areas of the brain; (iv) sight and hearing; (v) the electrical activity of the brain; (vi) recognition and mental events.

This little volume comprises the six Waynflete lectures delivered by Professor Adrian in Magdalen College, Oxford, in 1946. They are written for the enlightened layman, in that fluent style of his which by its simplicity of expression and modesty of exposition leads the reader to assume that to reveal all this was simple, and to synthesize the evidence revealed, easy. In point of fact the volume contains an account of Professor Adrian's recent original work on the excitable cerebral cortex, much of which has been published in *Brain* and the *Journal of Physiology* in the past few years.

He relates, within the limits of our knowledge, the representation of sensory function at the periphery and cerebral cortex and links the form of his representation to the biological importance of that function to the particular animal under review. From this he goes on to an account of the integration of the cerebral activity subserving the special senses, and to a discussion upon the meaning of the apparently spontaneous electrical rhythms which can be recorded from the brain. He ends with an essay on learning and memory.

Even those who are well versed in the electro-physiology of the central nervous system would do well to pause for a time and ponder the integration of evidence which this monograph represents. Those less directly concerned will be fascinated.

Denis Williams

1257 Anatomical Pattern as the Essential Basis of Sensory Discrimination: being the Forty-ninth Robert Boyle Lecture

W. E. Le Gros Clark. Oxford, Blackwell Scientific Publications [1947]. 16 pages. 22 x 14 cm. 1s. [£0.05]

Professor Le Gros Clark's Boyle lecture contains a combination of new information and speculation that makes it a very good shillingsworth for medical men, biologists, philosophers or any others interested in the problems of perception. He first summarizes some recent work on the arrangement of the nervous pathways connected with some of the sense organs. The earlier neurologists were content to describe the connexions between receptor and central nervous system and the pathways within the latter. The lines of two paths thus became very well known, and it was commonly supposed that anatomical investigation of these matters was now " complete ". More recently neurologists, largely under the leadership of Le Gros Clark himself, have realized that the details of the arrangement of nerve fibres within the pathway and centres may be of the utmost importance. In some cases (e.g. the eye and ear), there is a point-to-point connexion between individual organs of the receptor surface and parts of the brain. But the distribution of the points relative to each other is not the same centrally and peripherally; there is an elaborate sorting on the way inwards. It is now becoming clear that the detailed arrangement of these connexions with the projection area is a matter of very great importance for the functioning of the sensory system. Here is a vast new field for

the anatomist to explore and this is a beautiful example of the truth that a study seems to be complete only when those who pursue it have not sufficient imagination to carry it further. The detailed study of the connexions of the sensory fields will claim the attention of anatomists and histologists for many years, especially as physiologists, using the clues provided by the anatomical studies, come to investigate the processes going on in these areas, and in turn suggest further studies of the distribution of the various elements.

At the end of his lecture, Le Gros Clark deals with a problem perhaps even more fascinating—how all these extremely specific connexions come to be made during development. Discarding the theory that growing nerve-fibres are directed by chemical influences, he suggests, following Weiss, that they are controlled by the ultra-structure of the matrix in which they grow. It might be added that recent workers, Beams and Marsh, have revived an older idea that electrical potential gradients influence the direction of growth and the whole question remains very open. As Le Gros Clark points out, the view that fibres grow along surfaces only pushes the problem back to a consideration of "the incredibly complicated ultra-structural pattern of the substratum in the early embryo". He points out that this, like all living patterns, is not a static anatomical unit, but is only "mirrored" in a continually-changing substratum, as is a reflexion in a running stream. The analogy is telling enough but it is startling to find him pursuing it in a final sentence to the question: "What is the living body a reflection *of*?" There is evidently material here for much discussion and thought, and the lecture is an excellent example of the stimulus that can be obtained by combining accurate observation with imaginative thinking.

J. Z. Young

1258 Diseases of the Basal Ganglia and Subthalamic Nuclei

D. Denny-Brown. New York, Oxford University Press; London, Geoffrey Cumberlege, 1946. [Reprinted from Oxford Loose-Leaf Medicine] iv + 116 pages; 4 illustrations. 24 x 16 cm. 12s. 6d. [£0.625]

This short monograph is Dr. Denny-Brown's contribution to the Oxford Loose-Leaf Medicine, republished separately. In it, the author has collected all the major contributions to our knowledge of this corner of neurology.

The sections in which he deals with the symptomatology of the major and minor syndromes caused by disorders of the basal ganglia are accurate, lucid and pleasant to read. The most important part of the monograph, however, is the introduction, in which the underlying anatomy and physiology of the disturbances are synthesized in a manner characteristic of the Sherringtonian school of neurology.

This chapter of a well-known medical textbook is in the first rank of descriptive medical writing.

1259 Sensory Mechanisms of the Retina with an Appendix on Electroretinography

Ragnar Granit. London, Geoffrey Cumberlege, Oxford University Press, 1947. xxiii + 412 pages; 178 illustrations. 22 × 14 cm. £1 15s. [£1.75]

Section I. The electrical signs of excitation and inhibition in the retina and optic nerve. (i) The generation and inhibition of a rhythmic discharge in peripheral nerve. The nerve as a model sense organ; (ii) the electroretinogram and optic nerve response of some simple types of retina; (iii) the components of the vertebrate electroretinogram; (iv) the resting potential. Some further properties of the component potentials of the electroretinogram; (v) some characteristic properties of the discharge in isolated fibres of the optic nerve; (vi) the component potentials in relation to excitation and inhibition: summary of chapters i-v. Section II. The properties of rods and cones. Variations in area, intensity and duration of the stimulus in dark and light adaptation. "Flicker." (vii) The duplex nature of the retina as reflected in the electroretinogram; (viii) differentiation velocity as a function of the state of adaptation. The response to intermittent illumination; (ix) quantitative effects of variations in the strength of the stimulus; (x) the duplicity theory from the electrophysiological point of view. E- and I-retinas defined. Summary of chapters vii-ix; (xi) interaction. Area, duration and intensity of the stimulus as interchangeable variables; (xii) some other forms of interaction. Synchronization. Section III. The properties of the photosensitive substances and the mechanism of excitation. (xiii) The absorption spectrum of visual purple and its photoproducts. Visual violet; (xiv) chemical aspects of the problem. The significance of vitamin A; (xv) the regeneration of visual purple; (xvi) the photochemistry of visual purple. The spectral distribution of its sensitivity and the scotopic luminosity curve; (xvii) light and dark adaptation. Section IV. Colour reception. (xviii) The nature and history of the problem: (xix) colour receptors in different types of retina; (xx) the dominator-modulator theory; (xxi) the composite nature of the photopic dominator system, the mammalian colour receptors; (xxii) the dominator-modulator theory and colour vision. Appendices. References. Author and subject indexes.

Newcomers to visual physiology are fortunate in that within recent months two modern contributors to this field of study—Dr. W. D. Wright and Professor Granit—have written monographs. Books of this kind not only lighten the reading of the novice, but also serve to underline and crystallize the views of the author upon vision as they stand today. Scientific papers do not always do this, because their appearance in print is often followed by maturer consideration, which may never achieve full weight except in a monograph of this kind.

Professor Granit's book is such a crystallization of views and, in addition, an extensive digest of the author's own experimental work. It is a book which everyone interested in visual physiology should make a point of reading.

The work is divided into four sections. Section III gives a concise account of the physiology and biochemistry of visual purple and related photosensitive substances. The section explains all the names used by other workers and discusses the interrelationships of the various pigments. There is one chapter devoted to light and dark adaptation and the review of the photochemical aspects as a whole is one of the best in the literature.

Section IV deals with colour reception and in Chapter 20 the author's dominator-modulator theory is fully stated. This theory, as many people will know, is based upon action potential records obtained, by the author's own microelectrode technique, from single (or at most a few only) optic nerve fibres. It is a pity that the details of this technique are so poorly described. One felt that one would like to know much more of the actual method itself. In the final chapter the author links his work with that of those who investigate vision from the subjective aspect and this part of the book, which might well have become extremely speculative, is quite in balance with the rest of the matter. Here the importance of the electrophysiological approach to colour vision is stressed. It has revealed, for example, the presence of the photopic dominator type of response from a single fibre; this fibre has a spectral sensitivity curve which covers most of the spectrum and could not be of much use to the animal for wavelength discrimination. The author recalls that v. Kries and several others of the older workers realized the partial independence of the sensations of colour and brightness—an independence which they found difficult to harmonize with the trichromatic theory and which is easily explained by assuming that the photopic dominator is a brightness receptor.

Sections I and II deal with the author's work on the electroretinogram and other electrical behaviour of the retina and optic nerve. Although these sections provide a clear account of the work, the general reader will not find them easy to read. Here the author stresses the importance of correlating the nerve discharge with the electroretinogram.

There are 34 pages of references.

OTORHINOLARYNGOLOGY

1260 Lehrbuch der Hals-Nasen-Ohren- und Mundkrankheiten

Edited by *A. Barraud, F. R. Nager, L. Rüedi, E. Schlittler & J.-P. Taillens.* Basel, S. Karger, 1947. xii + 609 pages; 177 illustrations. 25 × 17 cm. Sw. fr. 60.

I. Allgemeiner Teil. (i) Allgemeine Untersuchungstechnik; (ii) spezielle Untersuchungsmethoden für Mundhöhle, Rachen, Nase, Kehlkopf und Ohr; Tracheo-Bronchoskopie und Ösophagoskopie; Röntgenuntersuchung, Diaphanoskopie. II. Spezieller Teil. (i) Die Erkrankungen der Mundhöhle; (ii) die Krankheiten des Rachens; (iii) die Erkrankungen der Speiseröhre; (iv) die Krankheiten der Nase und ihrer Nebenhöhlen; (v) die Krankheiten des Kehlkopfes; (vi) die Erkrankungen der Luftröhre und der Bronchien; (vii) Stimm- und Sprachstörungen; (viii) die Erkrankungen des Ohres; (ix) Innenohr und vegetatives Nervensystem; (x) Otoneurologie des Zentralnervensystems; (xi) die Vererbung in der Otolaryngologie. III. Die Bedeutung der Hals-Nasen-Ohrenheilkunde für die ärztliche Gutachtertätigkeit; Ohr und Schule; Hörapparate, soziale Fürsorge. (i) Hals-Nasen-Ohrenheilkunde und ärztliche Gutachtertätigkeit; (ii) Ohr und Schule (Schwerhörigenschule, Taubstummenanstalt); (iii) Hörapparate—soziale Fürsorge. IV. Rezeptsammlung. V. Sachregister. VI. Namenregister.

This swiss textbook must be welcomed as a notable modern treatise on the diseases of the mouth, throat, nose, larynx and ear. It is a first-rate textbook for students, and postgraduates and specialists too will find it a comprehensive work of reference. The importance of a background of general medicine is stressed throughout.

An excellent feature is an introduction on the taking of the case-history designed to disclose any condition which might give rise to ear, nose and throat symptoms. This is followed by a brief explanation of the meaning of the common ear, nose and throat symptoms and a clear outline of the special examinations; it seems unnecessary to show the Killian-Bruning endoscopes, while mentioning in the text that the distally illuminated tubes are extensively used.

The arrangement of subject-matter is excellent. The same plan is followed as far as possible in all diseases: etiology, pathology, diagnosis and treatment are discussed in turn. There are no descriptions of operations, since these are regarded as the province of specialists. The exceptions to this are very clear descriptions of laryngotomy and tracheotomy, and of intubation.

The *Mouth* is dealt with first; a feature here is the tabulation of the diseases due to hypovitaminosis and a description of the conditions due to poisoning with mercury, lead, gold, silver, arsenic and iodides.

The *Pharynx:* the tonsil and adenoid problem is discussed fully and very sound conclusions arrived at, which should be of great help to doctors. There is also a very good description of the various throat-affections consequent upon blood diseases.

The *Nose and Sinuses:* like all the rest, this section is full of highly practical advice. In the discussion on headache, extra-nasal causes are given as well as nasal, and the point made that if the application of cocaine to the middle turbinal diminishes the pain, the cause is probably in the nose or sinuses. Advice is given against the use of alum in the nose, as it has a specific toxic action on the olfactory nerve.

In dealing with epistaxis no mention is made of the recently-suggested ligature of the ethmoidal artery in uncontrolled cases. And there is no mention of calciferol in the treatment of lupus.

The *Larynx, Trachea and Bronchi:* all comprehensively dealt with; the diagrams of the cords and their paralyses are good. It is of interest to read that in 1·5% of thyroidectomies, paralysis of one recurrent nerve occurs, and that bilateral paralysis occurs during or after operation, "especially if one cord was paralyzed before operation by the thyroid swelling." The coloured plate of laryngeal diseases is not so good as others.

The *Ear:* this part has set a very high standard to any competitor. Not only are the descriptions of the anatomy and pathology admirable, but they are illustrated by many reproductions of microscopical appearances of sections of the temporal bone, of great value to the reader. Every complication of acute and chronic inflammation is described and explained; indeed, there is a wealth of practical information, both for student and expert.

Every aspect of deafness is considered. The section dealing with deaf-mutes is fully illustrated to show the method of teaching lip-reading, and concludes with advice on their treatment as human beings and the help that can be given them by clubs and social service.

Throughout the work, treatment by sulpha drugs and penicillin is advocated, but there is no mention of methods of administration nor of dosage, and even today dosage is not standardized.

This is one of the best textbooks, if not the best, of the present day on the diseases of the speciality; it contains a great store of information in a most readable form.

W. M. Mollison

PATHOLOGY

1261 Lectures on the Liver and its Diseases: Comprising the Lowell Lectures Delivered at Boston, Massachusetts, in March 1947

H. P. Himsworth. Oxford, Blackwell Scientific Publications, 1947. xiii + 204 pages; 58 figures. 23 x 15 cm. 18s. 6d. [£0.925]

(i) The types of liver injury and their structural consequences; (ii) the vascular factor in liver injury; (iii) nutritional factors in liver injury: experimental; (iv) nutritional factors in liver injury: human; (v) noxious factors causing liver injury; (vi) the syndromes of hepatic failure; (vii) the clinical classification of liver disease; (viii) infiltration of the liver and post-infiltrative fibrosis; (ix) parenchymatous hepatitis; (x) cholangio-hepatitis, obstruction to the bile ducts, and biliary diffuse hepatic fibrosis, (xi) circulatory disorders; focal lesions; and cancer of the liver; (xii) conclusions. Index.

Within the past ten to fifteen years certain facts in the pathology of the liver have assumed a major importance. These are: (i) the possibility of producing extensive and fatal hepatic necrosis in experimental animals by manipulation of the diet; (ii) the possibility of producing extreme fatty change in animals by similar means; (iii) that such fatty change may be a precedent incident in cirrhosis of the liver; (iv) that certain "lipotropic" substances will prevent or abolish such fatty infiltration. It is the endeavour of the author to bring together these various observations, and to unite them in a relatively-simple concordant theory of liver pathology.

His first postulate is that liver necrosis is essentially an ischaemia, due to swelling of liver cells and obliteration of the sinusoids; his next is that hepatic necrosis is essentially of two types, differing fundamentally: the one, a "massive necrosis" of irregular large areas of liver with no particular anatomical distribution (save that the left lobe is liable to suffer more than the right); and the other, a "zonal necrosis", i.e. an anatomically defined necrosis limited to lobules, affecting them all, but not confluent. This difference is pushed further into the chronic stage, or stage of partial recovery, so that the first lesion results in an irregularly scarred liver—"post necrotic scarring" (the nodular hyperplasia of other authors); and the second in a fibrosis destructive of lobular pattern—"diffuse hepatic fibrosis" (classical portal cirrhosis). These contentions are widely agreed, though the writer introduces a new terminology, but there is much that is new in the support of the argument by a large amount of experimental work, mainly, if not wholly, upon rats, which emphasizes with great clarity the distinction between the two pathological pictures. In this work Professor Himsworth was assisted by a pathological colleague, Dr. L. E. Glynn.

The results of this investigation show, broadly speaking, that the dietary deficiency which leads to massive liver necrosis is a lack of protein, and in particular the absence of the sulphur-containing amino-acids, methionine and cystine. It has frequently been observed that in acute necrosis of the liver the left lobe suffers more than the right and the ingenious explanation is put forward that as the right lobe receives principally blood from the small intestine, whereas the supply to the left lobe is largely admixed with blood from the splenic vein, it is to be expected that the former will receive amino-acids absorbed from the intestine in higher concentration, and thus suffer less when there is a specific deficiency of these in the diet. On the other hand, the lobular lesions which lead to a typical portal cirrhosis were found to be a sequel of gross and prolonged fatty infiltration of the liver; in the rats used for these experiments the fat content produced was between seven to fifteen times the normal, and this was maintained from 100 to 300 days, that is, for a period equivalent to about seven to twenty years of a man's lifetime. Such a condition is obviously an extreme one and it may legitimately be questioned how far such a result can be applied to explain the disease in man.

The experimental conditions producing this fatty change and subsequent fibrosis can also be shown to be dietetic, the condition being occasioned either by diets rich in fat, or by those deficient in "lipotropic" substances such as lecithine, choline, methionine and some others. In sum, the difference between these two forms of fibrosis and necrosis are: the massive form of the one and the lobular form of the other; the absence of notable fatty change in the one and its characteristic appearance in the other; the production of a fibrotic type of lesion, having the picture of nodular-type hyperplasia with large areas of regenerated liver in the one, and of portal cirrhosis, with an absence of recognizable liver lobules, in the other.

From this experimental and pathological study the author turns to human liver disease. It has long been known that fatty infiltration is a common feature of "alcoholic cirrhosis" but the exact relationship of the two conditions has been ill-understood. Professor Himsworth believes it to be a causal one, the liver cells, swollen by infiltrated fat, compressing the blood vessels and leading to a quiet disappearance of the liver parenchyma and an overgrowth of fibrous tissue, especially of the portal tracts. He further points out the high incidence of cirrhosis in certain coloured races in some parts of the world where alcohol is not apparently to blame and where dietary deficiency, especially

in the rather expensive protein substances we have considered, is widespread. This is often particularly marked in infancy and young adult life in the poorer native races, and a good case is made out for a dietetic cause for this fibrosis; likewise the incidence of primary hepatic cancer—something of a rarity in Western Europe, and a well-known complication of liver fibrosis with regenerative areas—is instanced to support the same argument. Alcoholic cirrhosis is explained on the ground of the effect of chronic gastritis on appetite and food-absorption, and the predilection of the chronic alcoholic for spending his money on drink rather than upon the lipotropic factors which are so good for him.

The argument we have sketched in its broad outline occupies about half the book and is of the greatest interest. It is not too easy to read and suffers from a certain amount of reiteration. The rest of the book is devoted to a less penetrating analysis of other diseases of the liver, with a sharp eye to the main thesis. Hepatitis, the effects and action of poisons, and the various manifestations of hepatic failure are analyzed. There is a strange statement under the heading which includes fatty infiltration that "the infiltrating material is confined to the parenchymal cells where it presumably is formed" which must not be taken too literally, and a dreadful heresy that amyloid disease comes into the class of "conditions in which the liver cells are distended by some substance which accumulates in their cytoplasm".

Professor Himsworth has written an extremely well-documented and stimulating book. He sagely remarks that "The progress of knowledge can be as effectively impeded by a misconceived hypothesis as by factual ignorance"; time will show what place in the Valhalla of medical theories awaits those put forward in his book. Be this as it may, clinicians and pathologists will be grateful for the material here assembled and appreciate the tenacious investigation which has led to these conclusions.

J. H. Dible

1262 Pathological Histology

Robertson F. Ogilvie. Third Edition. Edinburgh, E. & S. Livingstone Ltd., 1947. xii + 459 pages; 260 illustrations. 22 × 14 cm. £1 17s. 6d. [£1.875]

(i) Disturbances of nutrition; (ii) disturbances of the circulation; (iii) inflammation and repair; (iv) specific inflammations; (v) tumours; (vi) tumours (*continued*); (vii) circulatory system: blood vessels; (viii) circulatory system: heart; (ix) respiratory system; (x) alimentary system: stomach and intestines; (xi) alimentary system: liver and gall bladder: pancreas; (xii) urinary system; (xiii) reproductive system; (xiv) haemopoietic system; (xv) nervous system; (xvi) integumentary system; (xvii) locomotor system; (xviii) endocrine system. Index.

This book is now established as a reliable guide to the practical study of pathological histology. It contains 260 beautifully executed photomicrographs in colour of the histological changes accompanying all the more common disease processes. The colour rendering is faithful and the choice of magnification and fields has obviously been carried out by a teacher of this subject of wide experience. Each illustration is accompanied by an adequate legend and the text of the book contains commendably brief and lucid general descriptions of each process illustrated.

The book can be recommended as the best possible substitute for a demonstrator of pathology to the student who is working through his own collection of sections, and should be most valuable in these days when classes tend to be overcrowded and skilled demonstrators "in short supply".

G. Hadfield

1263 Pathology of Tumours

R. A. Willis. London, Butterworth & Co. (Publishers), Ltd., 1948. xxiii + 992 + 52 pages; 500 illustrations. 25 × 17 cm. £3 3s. [£3.15]

Part I. (i) Definition of tumour; (ii) classification and nomenclature; (iii) innocence and malignancy; (iv) experimental production of tumours; (v) statistical study of tumours; (vi) tumours in animals; (vii) the mode of origin of tumours; (viii) structure and growth of tumours; (ix) the direct spread of tumours; (x) metastasis; (xi) hypotheses as to the nature of neoplasia; (xii) recapitulation. Part II. (xiii) Epithelial tumours of the breast; (xiv) epithelial tumours of the skin; (xv) epidermoid carcinomas of the lips, mouth, pharynx and larynx; (xvi) tumours derived from the epithelium of the dental lamina; (xvii) epithelial tumours of the salivary glands; (xviii) epithelial tumours of the nasal and paranasal cavities; (xix) epithelial tumours of the trachea, bronchi and lung; (xx) carcinoma of the oesophagus; (xxi) carcinoma of the stomach; (xxii) epithelial tumours of the small intestine; (xxiii) carcinoma of the large intestine; (xxiv) carcinoma of the liver; (xxv) epithelial tumours of the biliary tract; (xxvi) epithelial tumours of the pancreas; (xxvii) adenoma and carcinoma of the kidney parenchyma; (xxviii) epithelial tumours of the urinary passages; (xxix) epithelial and related tumours of the ovary; (xxx) carcinoma of the Fallopian tube; (xxxi) epithelial tumours of the uterus; (xxxii) epithelial tumours of the vagina and vulva; (xxxiii) epithelial and related tumours of the testis and epididymis; (xxxiv) carcinoma of the prostate; (xxxv) epidermoid carcinoma of the penis and scrotum; (xxxvi) epithelial tumours of the thyroid gland; (xxxvii) epithelial tumours of the thymus; (xxxviii) epithelial pituitary and parapituitary tumours; (xxxix) tumours of the adrenal cortex; (xl) tumours of the parathyroid glands; (xli) introduction to mesenchymal tumours; fibroblastic tumours and myxomas; (xlii) tumours of adipose tissue; (xliii) tumours of cartilage and bone; (xliv) tumours of synovial tissues; (xlv) angiomas: tumours and tumour-like overgrowths of vascular tissue; (xlvi) meningioma or arachnoid fibroblastoma; (xlvii) leiomyoma and leiomyosarcoma; (xlviii) rhabdomyoma, rhabdomyosarcoma, and rhabdomyoblastic mixed tumours; (xlix) tumours of lymphoid tissue; (l) plasmocytomas and myelomatosis; (li) other neoplasms of haemopoietic tissues; (lii) the gliomata; (liii) papillary tumours of the choroid plexus; (liv) neurilemmoma and other tumours of nerve-sheaths; (lv) neuroblastoma and ganglioneuroma; (lvi) tumours of chromaffin tissues and of the carotid and aortic bodies; (lvii) neuro-ectodermal tumours of the retina and ciliary body; (lviii) the melanomata; (lix) chordoma; (lx) embryonic tumours of kidney and liver: and general comments on embryonic tumours; (lxi) the teratomata; (lxii) chorion-epithelioma.

The need for a new, comprehensive textbook on the pathology of tumours has been felt for a long time by workers in this particular field as well as by morbid anatomists in general. Without doubt, the *Pathology of tumours* by Professor R. A. Willis will go a long way towards meeting this need. Admirers of his former writings, especially of *The spread of tumours in the human body*, will know that his interest has for long been focussed on tumour pathology. In this book of over 1,000 pages, he brings the experience of years to bear upon our present knowledge of tumour problems. Thus we are presented with an extraordinarily able summary of other workers' opinions and findings, together with Professor Willis' own views, more often than not formed as a result of personal investigation and expressed in no uncertain terms. In consequence, it is hardly likely that all the views expressed will be accepted without reserve.

One-fifth of the book is devoted to general considerations and this includes a helpful and up-to-date chapter on the experimental production of tumours, a vast subject at this present time. The other four-fifths, i.e., the main part of the book, are concerned with the pathology of tumours in various organs, and describe systematically: (a) the epithelial tumours of the breast, skin, digestive and respiratory organs, genito-urinary system and ductless glands; (b) the tumours of mesenchymal tissues, skeletal, myeloid and nervous. The incidence according to site, age, sex, race and species is discussed, as well as causative factors, structure, growth, metastasis, etc. The short references to tumours in animals and the descriptions of personally-observed representative cases are useful. There is a final section on the melanomata, chordoma, embryonic tumours, teratomata and chorion-epithelioma. Not a few of these subjects, for example the epithelial tumours of the skin, the teratomata and testicular and ovarian tumours, have been the special interest of Professor Willis for many years. In all cases, a critical summary of the work of other authors is presented, and at the end of each chapter is a comprehensive bibliography, in which those papers which have been found to be particularly helpful and instructive are listed in large, heavy type, and the full title included. This original and selective method is much to be commended. "Whatever omissions I may be guilty of in my reference lists, I can at least claim that they comprise works which, with very few exceptions, I have personally consulted in the original". The illustrations, mostly photomicrographs and numbering 500, are all from personally studied material. The standard of reproduction is very high and the legends particularly valuable. The selection is, perhaps, a little arbitrary; for example, there are 15 photomicrographs of fibro-adenoma of the breast and none of Brenner tumour of the ovary.

Many of Professor Willis' views will command agreement from most pathologists. For instance, the chapters on epithelial tumours of the testis and ovary are excellent and summarize current opinions fairly and clearly. Other of his opinions are less easily accepted. He would dispense completely with the term "endothelioma" and would classify tumours of mesenchymal tissues which happen to possess surfaces, with other tumours of mesenchymal origin. He supports entirely the epidermal origin of the melanomata; his main objection to a neural origin "is that these lesions are, as already insisted, plainly of epidermal origin". This does not seem to be a very cogent argument. He regards Paget's disease of the nipple as a form of epidermal carcinoma in situ, contrary to the views of Muir and others.

This is a book which no pathologist can afford to be without. It is a mine of up-to-date information, is most readable and is a model of accuracy and good sense. In addition, it contains that element of provocation which stimulates the reader to further thought and reading.

Georgiana M. Bonser

PSYCHOLOGICAL MEDICINE

1264 Child Psychology

Arthur T. Jersild. · Third Edition. London, Staples Press Limited, 1947. xi + 623 pages; figures. 21 x 14 cm. £1 10s. [£1.5]

(i) Beginnings of behavior; (ii) some general characteristics of development; (iii) some aspects of living and learning in infancy and early childhood; (iv) motor development; (v) development of social behavior; (vi) development of social behavior (*continued*); (vii) feeling and emotion; (viii) feeling and emotion (*continued*); (ix) language development; (x) the growth of understanding; (xi) growth of understanding (*continued*); (xii) children's make-believe, dreams, and other imaginative activities; (xiii) children's ideals, morals, and religion; (xiv) children's interests; (xv) the growth and prediction of intelligence; (xvi) personality and problems of adjustment. Author index. Subject index.

There is a pressing need for a good textbook on child-psychology; and, within the limits that he has set himself, Professor Jersild's book may be warmly recommended as a sound and scientific review of the subject. The third edition has been largely re-written. It incorporates all the latest american work of any importance, and appends excellent bibliographies on the chief topics at the end of each chapter.

Professor Jersild's primary purpose is to present a clear picture of the development of the child's personality. He is interested more in the emotional, moral, and social aspects than in problems of intellectual growth. The chapter on intelligence is comparatively brief; and the book makes no attempt to discuss in any detail the nature and maturation of special intellectual capacities, as assessed by psychological or educational tests or studied by factorial procedures. These topics, however, have already been fairly well covered in previous publications. On the other hand, there is at the moment no other book which succeeds so well in summarizing what is known about the development of feelings, interests, and ideals.

Professor Jersild adheres to no single school of thought; and his treatment is at once critical and eclectic. His tabular summaries giving the results of questionnaires and other inquiries upon such topics as children's games, commoner modes of enjoyment, range of worldly knowledge, and the like, at successive years of life, are most informative; they serve admirably to remind the student how essential it is to check hypotheses by objective data. Unfortunately, most of the summaries relate to investigations carried out in the USA. Hence, the inferences drawn may not always apply to children on this side of the Atlantic. The very words used to describe the children's favourite games will be unfamiliar to many british readers. That, however, is almost unavoidable, since few researches of this type have been carried out on any extensive scale in Britain. It is to be hoped that this english issue of the book will stimulate british psychologists and research-workers to institute similar inquiries.

1265 The Shaping of Psychiatry by War

John Rawlings Rees. New York, W.W. Norton & Company, Inc., 1945. 158 pages. 21 × 14 cm. 10s. 6d. [£0.525]

(i) The frontiers extend; (ii) opportunities emerge; (iii) the way ahead. Appendix: The tasks of psychiatry. Index.

No one is better fitted than Dr. J. R. Rees to describe how british psychiatry adapted itself to the calls made upon it by war, since he was Consulting Psychiatrist to the British Army from 1939 to 1945 and was responsible for most of the organization of army psychiatry during this time.

In this book, which is in substance the Thomas Williams Salmon memorial lectures given by Dr. Rees to the New York Academy of Medicine, he gives a very clear explanation of how dullards in the Army tended to form a social-problem group until it was discovered that drafting them to the Pioneer Corps was both therapeutic for the men themselves and productive of effective units for the war effort. He tells us that war provides more opportunities for psychiatrists than for physicians, and that very soon the man-power problem brought to the front the importance of selection. A Directorate of Personnel Selection was set up by the War Office under the Adjutant-General shortly after the Admiralty had started its own selection service for the Navy. The Royal Air Force, which had its flying crew selection at the start of the war, only later used selection methods for its ground staff.

For officer selection, which had previously been done by the "magic eye" technique, three group projection tests were developed which, with questionnaires and an intelligence test, formed the battery used for each candidate. Follow-up statistics showed the superiority of scientific techniques to the older methods in this type of selection also.

Dr. Rees says that morale can almost be defined as mental health and shows how low morale is associated with high sickness- and high delinquency-rates, including absence without leave. Nevertheless discipline cannot replace morale. He describes the value of films and radio talks in keeping up the spirits of soldiers long absent from home, and in discussing rehabilitation he shows how progress is resulting in a move away from the formal occupational therapy of recent times to individual care and welfare work and he instances what has been done for the blind, the partially sighted and the limbless.

He believes that the psychiatrist's work should be done not only in the out-patient department of a hospital but also in connexion with instability, social unrest, morale, and in advising modifications of working conditions, on welfare and on the use of leisure, on training and allocation, etc. In order that this can be done, procedures, tests and techniques will have to be worked out and adequate staffs provided, including psychologists, sociologists and statisticians. We are warned that malcontents and subversives will be called "communists" or worse unless we are able to demonstrate that they are men who have been unwisely handled and who are reacting like rebellious and difficult children. Dr. Rees also warns psychiatry against its internal difficulties, and its "old men," and says that it is too much dominated by clinical interests, by psychoses, and by local government.

The book is most stimulating and in these days of planning it is highly desirable that it should be read by all who may have responsibilities for organizing the future mental health services of the country. Quotations such as "Psychiatric thought must become part of the ordinary approach to his tasks of every worker in the field of health and human relations," and "Psychiatry must be planning in a strategic manner for the mental health of the future," indicate the breadth of the author's conception of the future of psychiatry. Just as Dr. Rees was one of the few who could have organized army psychiatry for the needs of war, so we shall have to rely on him to convince a wider public of the contribution which psychiatry can make to the health of the community in time of peace.

J. G. Hamilton

PUBLIC HEALTH

1266 Handbook of Preventive Medicine (Air Ministry Publication 1269B)

Air Ministry. London, His Majesty's Stationery Office, 1946, reprinted 1947. vi + 213 pages; 42 illustrations. 23 x 15 cm. 7s. 6d. [£0.375]

(i) Personal hygiene; (ii) water; (iii) food and nutrition; (iv) environment; (v) conservancy; (vi) communicable diseases; (vii) disinfection and disinfestation. Index.

A valuable and comprehensive survey of preventive medicine is contained within the 213 closely printed pages of this handbook published by the Air Ministry. The Royal Air Force have the deserved reputation of doing things well; their practice of hygiene is of high standard. One has been impressed not only in reading this book, but also from first-hand observation, by the ingenious practical ways devised by medical officers of the RAF in overcoming difficult problems of hygiene. Although, in conformity with service traditions, no names of authors are given, it is obvious from the pages of this handbook that the authorities responsible for it are masters of their job in theory and practice. One can detect that an effective "brains trust" has been busy, and apart from its own resources has had access to the best of current teaching. The hard experience gained through years of peace and combat, through scenes and conditions even more varied

than Greenland's icy mountains and India's coral strand, from the sub-stratosphere to the Libyan deserts, is reflected in these pages.

The excellent Chapter IV (Environment) contains sections on effects of heat and cold, hygiene and sanitation, heating of camps, lighting and ventilation, all of which are first-class. It is good that Bedford's charts on "effective comfort zones" have been reproduced. The illustrations are clear, but few readers, one fears, will study the many tables.

Minor points which the reviewer does not like so much include: (i) The rather close type and the fact that it is difficult, with this style of binding, to read the end of the line on the left-hand page; this can be obviated to some extent by loosening the binding cord. (ii) Under the section of methods of dealing with head infestation it would be wise in a future edition to include methods using DDT and Gammexane, mentioned in a separate section, as well as the Lethane treatment prescribed. (iii) Not every authority would agree that for scabies it is "imperative" to have *two* treatments with benzyl benzoate. (iv) In the section on communicable diseases more direct statements regarding the source of infection in syphilis and gonorrhoea might be considered. (v) Most important of all, the subject of Health Education deserves a separate chapter. It is all important to gain the co-operation of every man and woman in the Forces, and a syllabus of talks, together with a description of modern methods of health education and the way of raising the ideas and ideals of service personnel, is very necessary. (vi) The chapter on personal hygiene might be enlarged and the instructions on tooth brushing extended to other aspects of personal hygiene. These are of the greatest importance to morale as well as to physical fitness.

At the price of three half-crowns this handbook is a marvel of cheapness, conciseness, and good teaching. Many public-health students, other than Service personnel, will gain the greatest benefit from its study.

J. L. Burn

1267 Recent Advances in Public Health

J. L. Burn. London, J. & A. Churchill Ltd., 1947. viii + 409 pages; 82 illustrations. 22 × 14 cm. £1 5s. [£1.25]

(i) Introductory. Public health and the individual: (ii) Public health nursing service; (iii) the care of mother and child; (iv) nursery care; (v) school health services; (vi) health education; (vii) mental health services; (viii) dental health services; (ix) medico-social services; (x) the handicapped child; (xi) the care of the family; (xii) welfare of the aged. Public health and the community: (xiii) Poverty and public health; (xiv) rehabilitation; (xv) health centres: (xvi) municipal foot health services; (xvii) rural epidemiology; (xviii) airborne infections; (xix) diphtheria immunisation; (xx) methods of vaccination against smallpox; (xxi) tuberculosis; (xxii) venereal disease; (xxiii) scabies; (xxiv) verminous infestation; (xxv) municipal ambulance service; (xxvi) co-operation of voluntary and municipal agencies; (xxvii) international health relations. Public health and the environment: (xxviii) Smokeless air; (xxix) water purification; (xxx) swimming bath water; (xxxi) milk. High temperature short time method of pasteurisation; (xxxii) food substitutes; (xxxiii) Garchey System of refuse disposal; (xxxiv) home safety; (xxxv) road safety; (xxxvi) cremation; (xxxvii) garden cities.

This book is much more than a survey of progress in Public Health in Britain during the last few years. Rather it may be described as an outline of the best elements of current practice of the Health Departments of the major local authorities. It is, however, no formal exposition of administrative methods, for scientific progress towards prevention of disease is always related to the practice described.

Dr. Burn is an outstanding member of the younger school of medical officers of health who have long developed their interest in social affairs and have refused to be diverted by onerous administrative duties. It is amply clear from this book that the forebodings of so many health officers at losing their hospital work and many of the personal health services, under the National Health Service Act, are not fully justified. The vast majority of the subjects dealt with in this book are still in the particular, if not exclusive, province of the medical officers of health.

Over half the book is devoted to the health of children and their mothers—a proper proportion for any exposition of preventive medicine. For the rest, there are chapters on rural epidemiology, tuberculosis, prevention of infectious disease, and other subjects concerning which public health authorities are taking action for the benefit of the community. The chapters on the physical environment as influencing the health of the people are relatively short, a welcome realization of the extent to which the balance of public-health activity has swung away from sanitation. Nevertheless, it is strange in a book on public health not to find a chapter on housing. Perhaps because of the virtual cessation of slum clearance due to the war, this subject of housing has passed into the background of the health officers' work. There is, of course, incidental reference to housing in many parts of the book and in a study confined to "recent advances" the author cannot cover every subject.

There is no other book which deals with these subjects from the point of view of a medical officer of health, so that reference will repeatedly be made to it by postgraduate students and practising health officers. It is therefore disappointing to find such an inadequate index. It is understood that the original index was much more comprehensive but that paper shortage finally determined a drastic reduction. This defect will no doubt be remedied in future editions.

Alan Carruth Stevenson

1268 Report of the County Medical Officer of Health and School Medical Officer for the Year 1946

London County Council. London, London County Council, 1947. 86 pages. 25 × 17 cm. 2s. [£0.1]

Annual reports of medical officers of health in this country are not on the whole very imaginative, nor are they light reading. Indeed, considering the care devoted to their preparation, and the masses of information, so significant to an understanding of social affairs which they contain, it is a great pity that the presentation is such as to deter the prospective reader. It must be said that this report of the County Medical Officer of Health of London is a good example of this tendency—packed with thought-provoking information but difficult, oh so difficult to read from cover to cover.

1946 was a very difficult year: a year of shortages of staff, particularly of nurses and hospital domestic workers; of work under difficult conditions in emergency or partly damaged buildings; and of housing shortages. During the year the population of the area of London County Council (L.C.C.) rose by 500,000 to 3,000,000, 75% of the pre-war population, and this did not decrease problems of accommodation in houses, schools or hospitals.

In spite of all this, the work of the health department was further developed and new enterprises were launched in several directions. The County home-midwifery service was greatly extended and gas/air anaethesia introduced in domiciliary midwifery practice. Even in the understaffed hospitals, the number of confinements increased above the pre-war figures. When so high a proportion of all confinements (probably about 50%) are conducted by one or other council service, the health department is entitled to credit for their share in the low maternal mortality of 1·26 per 1000 live births. Only 0·33 per 1000 of the total is accounted to puerperal sepsis. These are the lowest figures ever recorded and compare favourably with those for the rest of England and Wales.

Infant mortality also fell to a new low level of 38 per 1000 live births, and child mortalities at all higher ages were also lower, mainly due to decrease in incidence and case mortality of whooping cough, measles and diphtheria.

This tale of reduction of mortalities in different groups and from specific causes could be continued indefinitely; certainly as far as statistical indices are considered the health of all London continued to improve.

One of the interesting developments of hospital work in London during the war was the much closer co-operation of the voluntary and the "L.C.C." hospitals. This showed itself not only in grouping of specialist facilities in units staffed jointly but in mutually advantageous arrangements for the teaching of nurses and medical students. The war-time association of teaching hospitals and council hospitals has been so advantageous as to be continued since the war and it is now to be perpetuated by an arrangement under the National Health Service. By this the special privileges accorded to the governing bodies of teaching hospitals is to be extended to include associated hospitals. This excellent arrangement will allow the London teaching hospitals to have properly balanced teaching material for the medical students and for the better all-round experience of nurses.

The School Medical Service of the London County Council is an enormous undertaking also controlled by the County Medical Officer and directed by a Principal Medical Officer. London is by far the largest unit of School Medical Service in the world (334,784 pupils in 1946), and that service is severely handicapped by the

dreadful old school buildings and medical inspection rooms which are still all too common. By delegation of authority to five divisional medical officers some of the disadvantages of unwieldy size are avoided. In two ways the London school medical work is unique: a high proportion of medical inspection and treatment is carried out by part-time practitioners, and most of the follow-up work (done by school nurses elsewhere) is the responsibility of voluntary care committees. These two differences can hardly fail to mitigate the "official" atmosphere inevitable to such a large undertaking. Perhaps the best vindication of the service lies not in the many tables showing reductions of incidence of this disease or that, but in the figure of 72·9 % which is the proportion of routine inspections at which the child's parent was present in response to invitation.

Nearly half of all children have their midday meal in school and 93·14 % of children in primary schools have one-third of a pint of milk free each day.

It is quite impossible to abstract further these eighty-three pages of closely packed information or even to mention the many activities of the London County Council special clinics, hospitals and schools. Perhaps enough has been said to convince a doctor interested in social medicine who is visiting London that he should try to see personally some of the activities of its Health Department.

A. C. Stevenson

RADIOLOGY

1269 Certain Aspects of the Action of Radiation on Living Cells

British Journal of Radiology. London, British Institute of Radiology, 1947. (Supplement No. 1. Report of London Conference held May 13–14, 1946.) 146 pages; illustrations. 25 x 18 cm. 15s. 6d. [£0.775]

First Session: A. A brief survey of the physical processes involved in the absorption of radiation by living cells. B. The action of radiation on viruses. Second Session: The action of radiation on dilute aqueous solutions. Third Session: The action of radiation on chromosomes. Fourth Session: The effects of radiation on germ cells with special reference to man. Index.

The Editorial Board of the *British Journal of Radiology* is to be congratulated on its new departure—styled "Supplement No. 1"—which, in every way, adheres to the high standards of its parent journal. As its rather unwieldy title implies, the *Supplement* reports the proceedings of a two-day Conference held in May 1946, under the auspices of the British Institute of Radiology in London.

The mode of action of ionizing radiations was discussed by some 18 speakers, all men of eminence in their own spheres, who presented original papers on highly specialized subjects, covering the scientific hinterland of medicine. For this reason, the general medical reader may find the genetics and radiochemistry in this volume rather heavy going. However, there are at least two articles (on Viruses, by Dr. Roy Markham; and The Effect of Radiation on the Normal and Malignant Cell in Man, by Dr. P. C. Koller), which are of great general interest. The rest of the subjects are extremely important to radiologists, and especially to radiotherapists; and, of course, to those studying these special subjects, which I propose to review seriatim.

The Conference divided itself into five main headings. First, a comprehensive survey of the physics of radiation absorption: this is very well done and constitutes a summation of the advances of knowledge in this subject. After this, follow papers on the action of radiation in four special cases: Viruses; Dilute Aqueous Solutions; Chromosomes; and, finally, Germ Cells, with Special Reference to Man.

The section on viruses is of obvious importance in view of the role of viruses in the causation of tumours. It is interesting to note how we have advanced since the days when bacteriophages were the subject of controversy, and their discoverers subject to ridicule. Since that time, phages have been photographed with the electron microscope, and some have been shown to have a shape similar to a tadpole. Their discovery was made in England and France independently by Twort and d'Herelle. In the symposium under discussion are two papers by french workers on research done during the occupation of France. It was gratifying to find good general agreement on parallel work conducted independently in the two countries.

The section on Dilute Aqueous Solutions has important bearings for the radiotherapist, since every malignant cell is approximately 90 % water; and advances in this subject throw much light on the indirect effects of radiotherapy. This is particularly true of the effects on enzyme solutions, and one feels that a little more emphasis might have been placed on Mitchell's work on the conversion of ribose into desoxyribose nucleic acid.

The third section is mainly concerned with chromosome breakage and interchange, and is of a very high standard indeed; to the radiotherapist, Dr. Koller's paper will have an especial appeal.

The final section, on The Effects of Radiation on Germ Cells, includes a discussion on the occupational hazards of radiology, with particular regard to the fertility of workers in this field. Laboratory work is mainly carried out on the smaller mammals and on various insects (*Drosophila*, *Habrobracon*, and the like), and conclusions drawn from these creatures are not necessarily valid for the larger mammalia. Fortunately, the rather alarming conjectures of the geneticists concerning sub-fertility have not, as yet, been borne out in the human race. We are reassured to read in the discussion which followed this section, that in rabbits (the largest mammals represented in the experimental animals) several normal generations have been bred from spermatozoa irradiated with 50 r to 100 r.

However, there remains a wide field of research in this direction, and a comprehensive survey of the size and number of congenital abnormalities, occurring in families of *x*-ray workers of all classes, would seem to be desirable: this is too large a subject to be dealt with in this review, as are most of the important questions raised in these papers.

The whole Supplement deserves the highest praise, both in format and content. It is a really important work—the best thing of its kind yet published. Every radiotherapist should buy, beg, borrow or steal this book, which fills an important gap in the literature of this difficult subject.

It is to be hoped that further Supplements will follow, and that they will be bound in the stiffer cover that they deserve. My own copy is already becoming well dog-eared from constant use.

Ronald Hadden

1270 Radium Dosage. The Manchester System

Edited by *W. J. Meredith*. Edinburgh, E. & S. Livingstone, Ltd., 1947. vii + 124 pages; 38 figures; 4 plates. 25 × 19 cm. 15s. [£0.75]

Part I. Clinical aspects. (i) General introduction; (ii) mould treatments; (iii) rules for line-source applicator treatments; (iv) rules for cylinder mould treatments; (v) interstitial treatments; (vi) dosage for cancer of cervix uteri. Part II. Physical aspects. (vii) The physical basis of the planar mould and line source systems; (viii) physical basis of the cylinder mould system; (ix) the radiation field of a continuous cylindrical applicator; (x) physical aspects of the interstitial treatments system; (xi) the calculation of dosage and an additional distribution rule for cylindrical "volume" implantations with radium; (xii) the use of radiographs for dosage control in interstitial gamma-ray therapy. References. Index. Appendix I, II.

The Radium Dosage system developed and used at the Christie Hospital and Holt Radium Institute, Manchester, has become firmly established and its wide use in this country provides forcible testimony of its value and reliability.

The present volume is really a collection of the various papers published from Manchester during the past thirteen years on the subject of radium dosage systems. An attempt has been made to link up the papers in such a way that a single dosage system has been elaborated to cover all three types of radium technique, i.e., mould, intracavitary, and interstitial. The book, like several of the original papers, is divided into two sections—Part I Clinical, and Part II Physical.

The first part is clearly and simply written and is devoid of formidable mathematical formulae. The well-known dosage tables and distribution rules are given for each technique described and a series of well-illustrated examples is furnished, based on the use of the National Radium Commission Standard types of radium container. The original dosage-graphs are in an appendix to the book and are given in the form of tables. Also included in the Appendix are useful tables concerning radon, areas and circumferences of circles and volumes of cylinders.

Part II of the book, on physical aspects, will appeal chiefly to physicists or radiotherapists fortunate enough to possess the requisite knowledge of mathematics.

The compilation of the book was a very happy thought, as it makes available in compact form information which is of fundamental importance both to radiotherapists and others concerned with or in any way interested in radium therapy.

M. Lederman

RHEUMATISM

1271 Rheumatism and Soft Tissue Injuries

James Cyriax. London, Hamish Hamilton Medical Books, 1947. 410 pages; 101 figures; 107 plates. 24 x 16 cm. £2 2s. [£2.1]

(i) Traumatic and rheumatic inflammation; (ii) referred pain; (iii) neuritis and perineuritis; (iv) the diagnosis of soft-tissue lesions; (v) the head, neck and scapular area; (vi) the shoulder region; (vii) the elbow, wrist and hand; (viii) thorax and abdominal wall; (ix) the alimentary tract; (x) diagnosis in backache; (xi) the treatment of bachache; (xii) the sacro-iliac joint; (xiii) pain in the buttock and thigh; (xiv) the lumbar nerve-roots; (xv) the knee; (xvi) the leg, ankle and foot; (xvii) treatment by movement (1); (xviii) treatment by movement (2); (xix) anaesthesia and analgesia; (xx) functional pain; (xxi) the problem of rheumatism and non-specific arthritis; (xxii) doctor and physiotherapist. References. Index.

This book contains the author's views on soft tissue injuries and rheumatism. In spite of its name comparatively little consideration is devoted to the latter subject. Some of the views expressed are somewhat unorthodox and the pathological conceptions will be generally considered over-simple.

The technique of massage which is particularly associated with the author's name is well described, and the greater part of the book consists in an account of its application to the various parts of the body, which are classified topographically.

There are many good illustrations and the volume is beautifully produced. It is likely to be of more interest perhaps to specialist physicians and physiotherapists than to the rank and file, but it provides food for thought for all.

W. S. C. Copeman

STERILITY

1272 Diagnosis in Sterility. The Proceedings of a Conference sponsored by the National Committee on Maternal Health, New York City

Edited by Earl T. Engle. Oxford, Blackwell Scientific Publications Ltd., 1947. xi + 237 pages; 43 illustrations. 23 × 15 cm. £1 5s. [£1.25]

(i) The semen specimen. Laboratory examination; (ii) clinical interpretation of the semen analysis; (iii) the testicular biopsy. A five-year survey; (iv) the role of the accessory glands in fertility; (v) chronic hemospermia. Origin of the bleeding and treatment with estrogen; (vi) diagnosing the endometrial biopsy; (vii) interpretation of the basal body temperature curves; (viii) interpretation of post-coital examinations of cervical mucus; (ix) history taking for the infertile couple; (x) an interpretation and evaluation of tubal patency tests; (xi) reflections on a working hypothesis concerning a mechanism of sterility; (xii) so-called "pelvic congestion" in relation to sterility; (xiii) summary of the conference.

The Proceedings of the Conference on problems of human fertility held under the auspices of the National Committee on Maternal Health, in January 1945, are presented in this volume.

Five papers on the male factors—the semen specimen (J. MacLeod), its clinical interpretation (F. A. Simmons), testicular biopsy (C. W. Charny), the role of the accessory glands in fertility (C. Huggins), and chronic haemospermia (D. F. McDonald)—were read and discussed. The seven papers on the female aspect were: endometrial biopsy and its diagnosis (A. T. Hertig), basal body temperature curves (P. Tomkins), the post-coital test (W. W. Williams), history taking for the subfertile couple (W. H. Cary), tubal patency tests (N. F. Miller), a working hypothesis of the mechanism of sterility (A. T. Kenyon) and "pelvic congestion" in relation to sterility (H. C. Taylor). Finally, one of the leading authorities on the subject—Dr. John Rock—gave a clear and succinct summary of the Conference. Three of the points from the various papers that he stressed were: the diagnosis of necrospermia is not usually a very important one, the need for a larger series of examinations of actively-procreating men in order to crystallize the various reference points for the consideration of semen, and the need for tactful handling of the husbands as there is so little to be done about very defective males.

On the female side, Dr. Rock said he was far from being impressed by the various treatments suggested to produce ovulation among the 3 to 5 per cent. of women who come to sterility clinics and are found to be anovulatory. Of mittelschmerz, it was still uncertain whether it came during the enlargement of the follicle when the cortex is being stretched, or when the cortex breaks, or with the impact of bleeding on the peritoneum. Of certain of his own cases he says: "I have come to the point of offering exploratory operation to any couple whose mating has been infertile for five years, and in whom there is no demonstrable cause for sterility. I will try a few endocrines here and there for two to three months, while they are making up their minds, but I think there is a great field for careful surgery in these cases."

The above papers, each followed by free and thorough discussions, go to comprise this volume of the Proceedings, which covers the various aspects of the subfertility problem.

Since this meeting there have been two more recent conferences under the aegis of the American Society for the Study of Sterility in June 1947, and February 1948. At the former, research on hyaluronidase, an enzyme of the mammalian testes and sperm, came prominently into the limelight. The Proceedings of the latter meeting have not yet been published, so that the degree of progress made since the 1945 Proceedings under review is difficult to assess, though there are many gaps in our present knowledge and much scope for research.

Cedric Lane Roberts

SURGERY

1273 Surface and Radiological Anatomy for Students and General Practitioners

A. B. Appleton, W. J. Hamilton & Ivan C. C. Tchaperoff. Second Edition rewritten by A. B. Appleton, W. J. Hamilton & G. Simon. Cambridge, W. Heffer & Sons Limited, 1946. viii + 332 pages; 390 figures. 25 x 19 cm. £1 11s. 6d. [£1.575]

I. General Anatomy and Methods. II. The Upper Limb: (i) Shoulder and arm; (ii) elbow, forearm and hand; (iii) vessels and nerves. III. The Chest and Back: (iv) Thoracic wall; (v) thoracic contents; (vi) physical examination of the thorax; (vii) great vessels; (viii) oesophagus. IV. Abdomen: (ix) Abdominal wall; (x) physical examination of the abdomen; (xi) abdominal contents; (xii) perineum; (xiii) deep blood-vessels of the abdomen. V. Head and Neck: (xiv) General features; (xv) the neck; (xvi) special organs and regions; (xvii) vessels and nerves; (xviii) the brain and its associated vessels; (xix) radiology. VI. The Vertebral Column. VII. The Lower Limb: (xx) Buttock and thigh; (xxi) region of the knee; (xxii) leg and foot; (xxiii) vessels and nerves. Appendices. Index.

The second edition of this book, written by three distinguished teachers from one scottish and two London medical schools, offers a new and inspiring approach to the study of anatomy. The radiological exposition of the skeleton and internal structures presents anatomy from a new and curiously realistic viewpoint. The projection on the surface of the deeper structures and their relation to the bony landmarks of the living body are of particular value in applied and clinical anatomy. The work should be no less valuable to the anatomist than to the radiologist and the clinician. The body is treated systematically, and its formal anatomy is presented in a novel, striking, and eminently truthful way. Many of the diagrams are highly original and strike home the anatomical points which they illustrate in so dramatic a fashion, that anatomical statements which have, from too frequent repetition in purely anatomical works, lost to the student their freshness, regain life and interest. This is really three-dimensional anatomy.

The book will also be valuable to the radiologist as well as to the clinician or to the students of anatomy, for by anatomical exposition the radiologist, too, is reminded constantly that his study is a three-dimensional one, and that anatomical substance underlies the shadows on his film.

Ian Aird

1274 Ambulatory Proctology

Alfred J. Cantor. London, Hamish Hamilton Medical Books, 1946. xv + 524 pages; 281 figures. 24 x 16 cm. £2 2s. [£2.1]

(i) Clinical anatomy; (ii) diagnosis; (iii) anesthesia and analgesia; (iv) preoperative and postoperative management; (v) pediatric proctology; (vi) pruritus ani; (vii) cryptitis and papillitis; (viii) anorectal fistula; (ix) perianal and perirectal abscesses and infections; (x) anal ulcer; (xi) hemorrhoids; (xii) prolapse and procidentia; (xiii) colitis: diagnostic methods; (xiv) enterocolitis and colitis; (xv) ulcerative colitis; (xvi) bacillary dysentery; (xvii) tuberculosis; (xviii) lymphogranuloma venereum; (xix) venereal diseases; (xx) intestinal parasites; (xxi) constipation; (xxii) melanosis coli; (xxiii) diverticulosis and diverticulitis; (xxiv) benign tumours; (xxv) multiple adenoma; (xxvi) malignant neoplasms; (xxvii) pilonidal dimple, sinus, cyst, and abscess; (xxviii) coccygodynia; (xxix) rectal stricture and anal stenosis; (xxx) anal incontinence; (xxxi) foreign bodies and rectal trauma; (xxxii) electrosurgical techniques. Index.

It is curiously antithetical that in the USA where specialization is narrowing perhaps more rapidly than elsewhere, a book should be produced which seems to make a specialty more accessible to the general physician. At first sight it would seem that it is a pity to distinguish arbitrarily those diseases in any field which require hospitalization from those which do not. The volume must perhaps be regarded rather as an argued plea for the more frequent treatment of rectal diseases in the consulting room. It is precisely in this particular that the book will meet with some criticism from british proctologists. There are no doubt advantages to be gained from the ambulatory post-operative treatment of certain rectal conditions, since the erect posture certainly allows for a free drainage, but in illustrating extensive and complicated procedures such as the treatment of deep pararectal abscesses in a book with this title, the author is perhaps inclined to treat rather lightly a most distressing and recurrent variety of ill-health, and one in which an inadequate operation is almost certain to fail in its purpose. Even the operation of haemorrhoidectomy is fully considered and three methods are described for use presumably in the ambulant patient.

The therapeutic measures described in the volume are, however, considered in such detail that it makes one wish that the author had not restricted himself to the ambulatory branch of his specialty. Diagnostic methods, too, are dealt with in the most satisfying fashion and, as a guide to rectal diagnosis and a manual of minor treatment, the volume is well worth its place in the practitioner's library.

Ian Aird

1275 British Surgical Practice. Volume 1

Under the general editorship of *Ernest Rock Carling* & *J. Paterson Ross.* London, Butterworth & Co., Ltd., 1947. xxxi + 536 pages; 228 illustrations; 2 plates. 25 x 17 cm. £3

(i) Abdominal emergencies; (ii) abdominal pain; (iii) abdominal wall; (iv) abortion; (v) abscess; (vi) achlorhydria and appetite; (vii) acidosis; (viii) actinomycosis; (ix) adhesions and cicatricial stenoses; (x) adhesions (pleural) in pulmonary tuberculosis; (xi) adiposity; (xii) adrenal glands; (xiii) after-care—introduction; (xiv) after-care—follow-up; (xv) after-care—methods and value of massage; (xvi) after-care—on return home; (xvii) after-care—post-operative; (xviii) after-care—remedial and occupational therapy and rehabilitation; (xix) air passages; (xx) allergy; (xxi) amoebiasis—amoebic infection of intestine (pathology); (xxii) amoebiasis—amoebic infection of intestine (surgery); (xxiii) amoebiasis—liver abscess and pathology of amoebiasis other than intestinal; (xxiv) amputations; (xxv) amyloid infiltration (amyloidosis); (xxvi) anaesthesia—general; (xxvii) anaesthia—local infiltration; (xxviii) anaesthesia—regional; (xxix) anaesthesia—spinal; (xxx) angina pectoris; (xxxi) angioma; (xxxii) anthrax; (xxxiii) anus, artificial (management); (xxxiv) anxiety states; (xxxv) appendicitis, acute; (xxxvi) appendix—tumours of; (xxxvii) arteries; (xxxviii) arthritis; (xxxix) artificial limbs; (xl) artificial pneumothorax; (xli) asepsis and antisepsis; (xlii) asymmetry; (xliii) autonomic nervous system—introduction; (xliv) autonomic nervous system—anatomy; (xlv) autonomic nervous system—arteries. Index to Volume 1.

This work, which was begun during the difficult days of the war, has been awaited with eagerness and, if we are to judge by this first volume, will now be welcomed by many open bookcases. It is a first-rate presentation of modern british surgical practice. The names of the editors-in-chief are sufficient guarantee that the material is all up-to-date, accurate and well arranged, and a perusal of any or all of the articles confirms this view.

The arrangement of the articles is alphabetical and this volume deals only with the letter A, but in it are included many important and valuable contributions. The two sections dealing with the surgery of the arteries (by Learmonth & Telford), that on arthritis (by Norman Capener), and on appendicitis (by Nuttall) are outstanding contributions. Excellent too are the articles on anaesthetics, on amputations and on aftercare. The last-mentioned subject is dealt with from every aspect by a group of experts. There is a short 6-paged section by Dr. Lindsey Batten entitled "On return home" which particularly appealed to the reviewer as showing such sanity and common-sense as is too often absent in the rush of surgical work. We would recommend every young (and also older) surgeon to read and re-read this short section, for it may do his patients good.

The illustrations are excellent and help the text considerably. Sufficient references are given to point the reader to more extensive accounts of the subject under review.

The editors-in-chief have taken a wide view of the subject and have called in several physicians to help their surgical colleagues.

The index is elaborate and, if anything, errs somewhat on the side of profuseness, but that is in the right direction. However, we think a certain amount of valuable space is wasted in several instances by the long initial list of headings at the beginning of each article. Readers of this volume will have their appetites whetted for the future instalments of this comprehensive and valuable work.

V. Z. C.

1276 A Synopsis of Orthopaedic Surgery

A. David Le Vay. London, H. K. Lewis & Co. Ltd., 1947. vii + 242 pages; 55 illustrations. 23 x 16 cm. 15s. [£0.75]

(i) Systemic skeletal diseases: disorders of osteogenesis; (ii) systemic skeletal diseases: disorders of adult bone; (iii) local diseases of bone: inflammatory; (iv) local diseases of bone: neoplastic; (v) affections of joints: non-tuberculous; (vi) affections of joints: tuberculous; (vii) skull, spine, pelvis; (viii) neck, shoulder, arm, hand; (ix) hip and femur; (x) knee; (xi) leg and foot; (xii) neurological disorders. Index.

Synopses in general have a limited appeal. There are many students who find difficulty in assimilating such a mass of concentrated facts. A synopsis of orthopaedic surgery, moreover, if wrongly directed and used is a potentially dangerous form of teaching; for in this speciality, perhaps more than in any other branch of surgery, a knowledge of the facts forms only a part of the necessary equipment. The development of a sound and balanced judgement in the choice of treatment and a knowledge of the imperative necessity for detailed supervision of after-treatment are of supreme importance. To accumulate a mass of facts from a synopsis while neglecting the development of such a balanced judgement, often leads to the knowledge being misapplied.

Mr. Le Vay is clearly well aware of these difficulties. In his preface he warns the reader that in assimilating the facts presented he must not lose sight of the necessity for considering each patient as an individual problem, to be individually assessed from every aspect, before deciding on a plan of treatment. His book is addressed only to the more senior undergraduate, and to the postgraduate student reading for the higher examinations. This is wisely so, for to read it with advantage the student must have already attained a reasonable standard of orthopaedic knowledge and should have had some experience in the orthopaedic wards and the out-patient department.

To those who fall into this category the book will undoubtedly prove of very great value. For its size it is remarkably complete and right up to date. This is particularly noticeable in those sections dealing with some of the more difficult orthopaedic problems, closely studied and now properly understood only in comparatively recent times. Such conditions as sciatica and low back pain, costo-clavicular compression, prolapsed cervical disc, and peripheral nerve injuries have been dealt with in a well-balanced, logical manner. The conclusions and recommendations are generally in accord with the most enlightened modern opinion. Indeed, there is very little in the subject-matter which calls for criticism.

In discussing the treatment of congenital talipes equinovarus in infants perhaps more mention might have been made of the use of plaster of Paris as a method of maintaining the over-corrected position. There are many surgeons who cannot accept the dogmatic assertion that wasting of the calf muscles results only from immobilization by plaster of Paris. Again, in the discussion on severed flexor tendons within the digital sheath, more stress might have been laid on the desirability of avoiding suture of the tendon within the length of the fibrous sheath, and of using a long graft in order to place the suture-lines at the proximal and distal extremities of the sheath.

Illustrations have been avoided except where considered essential for clarity. Those included are in the form of simple line-drawings and are adequate for their purpose. That depicting the vertebral displacement in spondylolisthesis is misleading, for the fifth lumber body is shown displaced forwards in relation to the fourth lumbar body as well as to the sacrum.

Except for the irritating frequency with which sentences are begun with a conjunction, and for an unwarranted looseness of terminology, such as the use of the word tubercle for tuberculosis, the style is easy to read; particularly so for a synopsis.

The author is to be congratulated on having produced a comprehensive and balanced summary of a relatively-new and constantly-advancing speciality in such a small compass.

H. Osmond-Clarke

1277 The Appendix

R. J. McNeill Love. London, H. K. Lewis & Co. Ltd., 1947. 186 pages ; 54 illustrations. 19 x 12 cm. 12s. 6d. [£0.625]

(i) Historical; (ii) anatomy; (iii) aetiology; (iv) diagnosis; (v) differential diagnosis; (vi) treatment of the appendix mass, and general peritonitis; (vii) appendicectomy; (viii) post-operative complications; (ix) appendicostomy; (x) chronic appendicitis; (xi) less common diseases of the appendix; (xii) obstetrical and gynaecological considerations. Index.

Nearly every year sees some new book on the appendix published, and this is quite as it should be, for appendicitis accounts for more acute abdominal emergencies than all other causes put together, and advances in treatment are constantly being made.

This little book by a well-known surgical author is well produced and racily written, and in a brief compass of twelve short chapters gives the essential facts as to the clinical symptoms, diagnosis and treatment of the various disorders of the vermiform appendix. We can recommend it as a sound presentation of present-day views, with that slight emphasis on the so-called " delayed " operative treatment which is perhaps needed as an antidote to the " immediate operation in every case " attitude.

We have little to criticize, but in two points we are not in complete agreement with the author. We have found that the triangle of hyperaesthesia in acute appendicitis is not like that in fig. 12 but has a horizontal upper limit at the level of the umbilicus; sometimes when the appendix has perforated the hyperaesthesia does not extend up so far. The second point is concerning the treatment of actinomycosis in the appendix region. The author states that " massive doses of penicillin are worthy of trial ". We should go further than this and say that large doses of penicillin should be continued without intermission for several weeks at least. If this be done the actinomycotic mass will very likely gradually disappear completely. In any case there ought never be the need to perform any excision or short-circuit.

The author rightly points out that pseudo-myxoma of the peritoneum may be caused by a persisting perforation of the appendix; the reviewer vividly remembers a case in which a male patient presented himself with a large mass filling the pelvis and causing a supra-pubic tumour which simulated a distended bladder. This proved to be a large pseudo-myxomatous mass which had its origin in a chronic perforation of the vermiform appendix.

We should like to see a reference to Willard Parker in the first (historical) chapter, and we were sorry to see Ochsner's name spelt wrongly in six places.

The reader of this book will learn a few facts of general information, e.g. how the north american Indian wakes up a sleeping person, and why unmarried women sometimes ask to have their appendix removed.

V. Zachary Cope

1278 Chronic Structural Low Backache due to Low-back Structural Derangement

R. A. Roberts. London, H. K. Lewis & Co. Ltd., 1947. v + 105 pages ; 46 plates. 25 x 19 cm. £2 5s. [£2.25]

(i) Defective ossification of the Pars Interarticularis; (ii) group A: cases of " spondylolisthesis "; (iii) group B: cases of " spondylolysis "; (iv) group C: cases of " unilateral spondylolysis "; (v) group D: cases with upper lumbar defects; (vi) group E: cases with radiological evidence of defects of ossification in the articular processes; (vii) group F: cases with various radiological changes; (viii) group G: cases with no definitely recognisable radiological changes; (ix) the significance of defects of ossification in the neural arch; (x) the significance of the histories of chronic backaches; (xi) the significance of oedema in over-strained soft tissues; (xii) neuro-vascular and " visceral " symptoms; (xiii) low-back structural derangement; (xiv) treatment from the structural aspect; (xv) the medical profession and the chronic backache. Index.

Chronic structural low backache is, in this book, attributed mainly to abnormalities of the " pars interarticularis "—conditions known as spondylolysis and spondylolisthesis. It is suggested that these abnormalities are much more frequent than is generally appreciated. Many figures are quoted to support this view. Another reason given for failure to recognize these structural derangements is that frequently they are visible *only* in *x*-ray plates taken obliquely. An interesting contention is that these defects are not due to failure of fusion but to " deossification " as a result of chronic strain. The symptoms are attributed to the chronic strain, of which the structural derangement is a manifestation. Considerable importance is attached to oedema as a cause of localized pain in the back and also of root pain. Relief following saline injections—said by some to invite a psychological rather than a physical explanation of the pain—is due to dilution of oedema, aiding its more rapid absorption.

There is nothing strikingly new in this book—except perhaps some points regarding the cause and significance of the laminar defects. The author quotes other writers who have emphasized the frequency of these defects and also that oblique views are necessary to see them. To say the book contains nothing new is, in a way, a form of praise, as a better interpretation of much that is already known is urgently needed.

There are 137 figures, all *x*-ray plates, showing various abnormalities of the pars interarticularis; many of these are traced for ease of interpretation.

The last chapter—comprising one fifth of the text—is a general attack on the attitude of the profession to sufferers from backache, and a particular attack on psychiatrists for convincing ignorant " orthopaedists " and others to swell the ranks of those suffering from so-called psychosomatic disorders. This is excellent, the best part of the book and probably what justified its production. There are no half tones in this chapter. The medical officer (or specialist) painstaking enough to record physical signs and make a diagnosis of one of the many causes of backache, including those mentioned by the author, does not exist. All neuropsychiatrists are psychiatrists only and have heard of " anxiety state ", but do not believe in physical signs in the diagnosis of disc lesions.

The book is interesting and stimulating. If it succeeds in making the profession as a whole more patient and interested in the considerable proportion of the population that suffers from backache it will serve a useful purpose.

J. C. Scott

TOXICOLOGY

1279 Poisons, their Isolation and Identification

Frank Bamford. Second Edition, revised by C. P. Stewart. London, J. & A. Churchill Ltd., 1947. viii + 304 pages ; 23 illustrations. 22 × 14 cm. £1 1s. [£1.05]

(i) Introduction : organization and equipment; (ii) classification of poisons; (iii) volatile poisons; (iv) volatile poisons (*continued*); (v) common metallic poisons; (vi) other metals; (vii) corrosive acids and alkalis; (viii) non-volatile organic poisons (alkaloids); (ix) non-basic organic poisons; (x) the isolation of non-volatile organic poisons; (xi) a systematic scheme for the identification of alkaloids; (xii) systematic testing for non-basic poisons; (xiii) miscellaneous poisons; (xiv) drugs of addiction. Index.

Soon after its publication in 1940, the first edition of this book had established itself as a reliable and most useful guide to the isolation and identification of poisons encountered in toxicological practice. The demands of chemists and clinical pathologists working in this field are exacting, methods must be described explicitly and must, above all, be of proven reliability. Bamford designed the volume as a practical handbook in which each test and procedure had been personally used in the examination of viscera for poisons and its ready acceptance as the standard british manual on the subject has indeed justified the high aims of the author.

In the second edition, under review, Dr. Stewart has faithfully preserved the book's outstanding characteristic. The text is little altered, the number of pages being indeed reduced by 40, but this is achieved by an addition of 5 more lines per page and the

exclusion of a separate author index. The short section on gaseous poisons is new and useful additional matter is noted under the quantitative determination of hydrocyanic acid, general procedures in toxicological analysis and under arsenic. A figure demonstrating the use of the Hartridge reversion spectroscope replaces that of the Duboscq colorimeter in the former edition. These are all improvements but, in the opinion of the reviewer, the value of the book has been enormously enhanced in this second edition by the judicious use of italics and sub-headings in bold type which facilitate quick reference and improve the general readability of the text. There is also evidence of careful trimming of several paragraphs with elimination of irrelevant matter, and the reviewer is glad to notice that the error in the chemical equation on p. 88 of the old edition has been perceived and corrected (p. 80).

Useful tabular rearrangement has been made of the barbiturates, and the section on the cardiac glycosides has been revised. The inclusion of notes on the preparation of reagents for alkaloid tests removes what was a blemish in the original work.

Altogether Dr. Stewart and the publishers are to be congratulated upon the high standard they have achieved and the book can be confidently recommended as essential on the shelves of any laboratory engaged in toxicological work.

C. Rimington

TOXICITY OF METABOLITES

1280 Detoxication Mechanisms. The Metabolism of Drugs and Allied Organic Compounds

R. Tecwyn Williams. London, Chapman & Hall Ltd., 1947. viii + 288 pages. 22 x 14 cm. £1 5s. [£1.25]

(i) Introductory and historical; (ii) the metabolism of some aliphatic compounds and cyclohexane derivatives; (iii) the metabolism of aromatic hydrocarbons; (iv) the metabolism of halogenated aromatic hydrocarbons; (v) the metabolism of phenols; (vi) the metabolism of aromatic alcohols, ethers, aldehydes, ketones and amides; (vii) the metabolism of aromatic acids; (viii) the metabolism of organic cyanides; (ix) the metabolism of the aromatic nitro, amino and azo compounds; (x) the metabolism of sulphones, sulphonic acids and sulphonamides; (xi) the metabolism of terpenes and camphors; (xii) the metabolism of heterocyclic compounds; (xiii) the metabolism of organic compounds of arsenic; (xiv) theoretical considerations and conclusions. Bibliography. General Index.

It is unfortunate that, by the use of the title *Detoxication mechanisms*, Dr. Williams has given new life to a misnomer which showed some sign of dying a natural death. The sub-title of this book, " the metabolism of drugs and allied organic compounds ", is at once a more satisfying terminology and a more true expression of the field covered by the author.

The aim of the author has been to summarize the literature over the whole field of drug metabolism for a period of just over one hundred years. The inevitable result is that the book, at times, assumes the character of a catalogue, albeit a most useful catalogue. Perhaps Dr. Williams might have held more readily the attention of the general biochemical reader as opposed to the specialist in his own field if he had brought his last chapter, Theoretical Considerations and Conclusions, to the beginning of his book and had then attempted to relate the detailed findings on individual compounds to his theoretical background. There is no doubt that he is right in rejecting both the chemical defence hypothesis and the surface tension hypothesis as a working basis for further progress, but there is too little indication, in the main body of the book, that the general metabolic pattern of the animal body is the governing factor controlling the fate of all metabolites, either natural or foreign. Surprisingly little information is given about kidney function and, on the whole, one is left with the impression that the animal has been regarded by many workers as an interesting toy capable of chopping complex molecules into curious shapes. Such comment is not so much a reflection on this book as upon the existence of an artificial barrier between intermediary metabolism and drug metabolism which was erected over a period of years by the concept of specialized detoxication mechanisms. Dr. Williams might have done more to destroy this barrier.

These are the criticisms of a general reader who found several chapters of this small book of 250 pages rather heavy reading; they do not detract from the value of the book as a source of information which, within the limits set by the author, is concise, clear and reasonably complete. The book has brought together much scattered information and will be useful to the teacher or to the research student entering the field; it will also save much searching of the literature by those workers who, without a detailed knowledge, suddenly find themselves faced with a problem in drug metabolism.

The book is provided with a general author index and a complete subject index which should make it a convenient source of reference. There are a few obvious printing errors and occasional formulae are badly printed or lack their full quota of bonds but on the whole the print is clear. It is unfortunate that the publishers should find it necessary to charge 25 shillings for a book of this size.

T. S. Work

TUBERCULOSIS

1281 Dust and its Effects on the Respiratory System

George H. Gill. London, H. K. Lewis & Co. Ltd., 1947. viii + 50 pages; 17 illustrations. 22 x 14 cm. 5s. [£0.25]

With such a vast amount of published work on this subject, much of it indeterminate or equivocal, confronting the author, it must have been extremely difficult for him to choose what to include or what to omit. Mr. Gill has come down on one or other side of the fence on some debatable points, but that could hardly have been avoided in a condensed work of this nature.

The terms " Pneumokoniosis " and " Silicosis " are always a pitfall: pneumokoniosis embraces all forms of dust disease in the lungs and at whatever stage of the disease, silicosis is a subdivision applied to the disease resulting from exposure to silica dust. " Pneumokoniosis of coal miners " is another subdivision applied to the disease resulting from exposure to coal dust in which it is assumed, however, that silica plays a part. Pneumokoniosis is not an early stage of silicosis.

Possibly emphysema could be better described as a condition in which the lungs, their elastic, contractile power having been destroyed, become over-distended with unused or useless air. Here one is confronted by the author's own problem of compressing information, however.

Mr. Gill's reference to the electron microscope is timely; possibly this instrument would clarify the present unsatisfactory assessment of dust hazard in coal mines.

Altogether the author is to be congratulated for encompassing in a short summary so much well-selected, concise and pertinent information. For those, lay or medical, interested in dust disease this is an excellent " Primer ".

E. Aslett

1282 Tuberkulöse Reinfektion beim Rinde und ihr Einfluss auf die Resistenz

E. Graüb, W. Zschokke, E. Saxer & H. Vonarburg. Basel, S. Karger, 1947. 82 pages; illustrations. 24 x 17 cm. Sw. fr. 12

(i) Einleitung; (ii) erste Versuchsperiode: 1932–1941; (iii) zweite Versuchsperiode: 1942–1947; (iv) Anhang.

Five calves subcutaneously infected with a bovine strain of attenuated virulence remained up to 4½ years resistant to subcutaneous infection with virulent strains. After subcutaneous infection with the avirulent bovine bacillus, a typical primary complex developed in three out of the five animals. One of the others showed bacilli only at the site of infection or in the regional lymph gland respectively. After virulent reinfection, however, a primary complex was found in one instance, whereas avirulent reinfection yielded only incomplete primary lesions, bacilli being recovered either from the site of reinfection or from a regional lymph node. After avirulent reinfection, latent tubercle bacilli were found in a lymph gland up to 24 months; after avirulent primary infection, up to 36 months at the site of infection. Repeated reinfection with a bovine strain of attenuated virulence proved a means of maintaining resistance to natural infection with virulent bacilli for years; (for example, 4 cows kept under observation for 4½–7½ years remained free of infection, in spite of immediate contact with tuberculous cows for 17–36 months). A local arrest of virulent bacilli at the site of reinfection could be demonstrated. They did not even reach the corresponding lymph glands. Animals infected with living avirulent bacilli became, as a rule, allergic and, although showing temporary fluctuation in the response, reacted to tuberculin—

the intradermal test being superior to the subcutaneous (thermo-) and ophthalmo-reaction. The subcutaneous test remains negative after spontaneous infection with human, avian and saprophytic acid-fast bacilli. A positive subcutaneous tuberculin reaction indicates infection with the bovine type. The subcutaneous reaction also depends upon natural or acquired resistance. With increasing resistance acquired by avirulent infection, tuberculin hypersensitivity vanishes, but may temporarily re-appear on the development of new active foci subsequent to avirulent reinfection. With regard to tuberculosis of the udder and infection of the milk, of the five calves infected with attenuated bacilli and reinfected in adult age, none developed chronic tuberculosis of the udder, at least within 4½ years, nor caused reinfection during pregnancy or lactation by any permanent excretion of tubercle bacilli through the milk, results which favour the conclusion that in infected cowsheds bacilli find their way into the milk after its excretion (for example, from infected faeces, vaginal mucus or infected straw-bedding).

The authors attribute the efficiency of avirulent infection, in inducing resistance, not only to the properties of the strain used, but also to their own *special technique*, consisting of repeated reinfection in *different* areas *involving ever-new groups of lymph glands*. If reinfections are always made in the same area the lymph glands already damaged by the first infection and previous reinfections will be unable to display their full tissue function in building up resistance (whatever this function may be).

An appendix deals with the question of the influence of pregnancy on reinfection. Out of four animals infected and reinfected with the avirulent strain, two were protected against virulent reinfection. The susceptibility of the two remaining animals is attributed to permanent excretion (during 1½ years) of *Brucella abortus* (Bang) with the milk, which predisposed the udder to infection—an observation which confirms the view of Roux, who regards Brucella infection as a general predisposition to udder-tuberculosis.

Finally, some experiments in guinea-pigs are reported which are supposed to show that avirulent infection, which leaves permanent changes at the site of infection, is superior in conferring resistance to virulent reinfection to those yielding none or only fugitive changes (as for example, with killed tubercle bacilli, "Antiphymatol", Friedmann bacilli and B.C.G. In this the authors fail to see that much depends here on the mode and frequency of application of the killed or avirulent bacilli, factors which they themselves have shown to be operative in their own experiments with cows, reported above.

W. Pagel

PARTICULARS OF BOOKS REVIEWED ELSEWHERE IN THIS NUMBER

The numerals in square brackets are the serial numbers of the articles in which these books are reviewed

[1210] Chemotherapeutic and Other Studies of Typhus

van den Ende, M. et al. London, His Majesty's Stationery Office, 1946. (Medical Research Council Special Report Series No. 255.) 246 pages; illustrations. 24 x 15 cm. 12s. 6d. [£0.625]

(i) The toxicity of two sulphonamides (V147 and V186) having activity against experimental typhus in mice; (ii) chemotherapeutic trials in typhus fever in man, and a report of the Naples typhus epidemic. A report of the British Army typhus research team; (iii) a quantitative test for neutralizing antibodies against typhus rickettsiae; (iv) comparison of typhus vaccines in the laboratory; (v) the antigenic structure of typhus rickettsiae. Appendix A: Illustrative case reports. Appendix B: List of drugs tested for chemotherapeutic activity against experimental typhus infection in mice.

[1211] Dimensions of Personality

H. J. Eysenck. London, Kegan Paul, Trench, Trubner & Co., Ltd., 1947. xi + 308 pages. 22 figures. 22 x 14 cm. £1.5s. [£1.25]

(i) Methods and definitions; (ii) assessments and ratings; (iii) physique and constitution; (iv) ability and efficiency; (v) suggestibility and hypnosis; (vi) appreciation and expression; (vii) synthesis and conclusions. Appendices. Bibliography and author index. Subject index.

[1213] Recherches Médicales en France Pendant la Guerre (1939-1945)

Jean Hamburger. [Paris], Editions Médicales Flammarion, 1947. 322 pages; illustrations. 25 x 16 cm.

[1214] Estudios Sobre el Pulmon Colapsado

José Abelló Pascual. Madrid, Publicaciones del Patronato Nacional Antituberculoso, 1947. 506 pages; illustrations. 24.5 x 17.5 cm.

[1214] Información sobre la Lucha Antituberculosa en España y Memoria Correspondiente al Año 1944

B. Benítez Franco. Madrid, Publicaciones del Patronato Nacional Antituberculoso, 1945. 366 pages; illustrations. 28 x 20 cm.

[1214] Estudio de las Contralateralizaciones, especialmente Precoces, en los Procesos Pulmonares Tuberculosos de Apariencia Radiologica Unilateral

F. Tello-Valdivieso. Madrid, Publicaciones del Patronato Nacional Antituberculoso, 1946. 77 pages. 52 illustrations. 25 x 18 cm.

[1214] La Tuberculosis Pulmonar Inadvertida y los Reconocimientos Radiologicos Seriados

José Zapatero. Madrid, Publicaciones del Patronato Nacional Antituberculoso, 1946. 119 pages. 25 x 17 cm.

[1214] La Lucha Antituberculosa en España

Madrid, Publicaciones Españolas. 40 pages. 50 illustrations. 22 x 19 cm. [no date]

[1215] Tercer Congreso Interamericano de Cirugía. Montevideo, 1-6 Octubre de 1946. Tomo I: Relatos y Co-Relatos Oficiales

Edited by *Fernando Etchegorry & Camilo Fabini.* Montevideo, Talleres Gráficos de A. Monteverde, 1946. xiii + 527 pages; illustrations. 24 x 17 cm.

[1215] Tercer Congreso Interamericano de Cirugía. Montevideo, 1-6 Octubre de 1946. Tomo II: Co-Relatos y Contribuciones a los Temas Oficiales

Edited by *Fernando Etchegorry & Camilo Fabini.* Montevideo, Talleres Gráficos de A. Monteverde, 1947. 582 pages; illustrations. 24 x 17 cm.

[1215] Tercer Congreso Interamericano de Cirugía. Montevideo, 1-6 Octubre de 1946. Tomo III: Asamblea de Delegados, Temas Libres y Crónicas

Edited by *Fernando Etchegorry & Camilo Fabini.* Montevideo, Talleres Gráficos de A. Monteverde, 1947. 662 pages; illustrations. 24 x 17 cm.

[1228] Wayfarers in Medicine

William Doolin. London, William Heinemann (Medical Books) Ltd., 1947. 284 pages; 39 illustrations. 22 x 14 cm. £1 1s. [£1.05]

(i) The oldest physician; (ii) the oldest textbook; (iii) *Graeculi esurientes*; (iv) medicine and the trade routes; (v) a mediaeval surgeon and his book; (vi) Leonardo, the forerunner; (vii) in the days of Vesalius; (viii) the anatomist in art; (ix) a patient of the Renaissance; (x) Montaigne; (xi) "honest little Harvey"; (xii) Descartes, the link; (xiii) "plain Parson Hales"; (xiv) some old journeyman surgeons; (xv) some antique stones; (xvi) the evolution of surgery; (xvii) early Edinburgh surgeons; (xviii) a surgeon of France; (xix) the resurrection-men; (xx) wayfarers in Canada; (xxi) Laennec; (xxii) Claude Bernard; (xxiii) Lister; (xxiv) Osler; (xxv) Gorgas; (xxvi) Sir Robert Jones; (xxvii) pathfinders in Dublin. Envoi: and the future? Appendix: bibliographical notes. Index.

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Shorter Notices

Ocular Vertical Deviations

J. Ringland Anderson. London, British Journal of Ophthalmology, Ltd., 1947. Monograph Supplement XII. 108 pages; 37 illustrations. 25 × 17 cm. 12s. 6d. [£0.625]

The author, ophthalmic surgeon to the Royal Albert Hospital, Melbourne, includes in this monograph "a partial survey of the literature and an analysis of a series of 402 patients with horizontal and vertical defects of the concomitant and paralytic types." He gives an account of the action of the main ocular muscles as an essential basis for diagnosis and stresses the need for attention to the co-ordinated movements of both eyes together in arriving at an accurate diagnosis. In making this diagnosis he considers the study of diplopia a most useful guide. He regards the frequency of the occurrence of anomalies of the vertically acting muscles as much underestimated and notes the frequency of finding disorder of the vertical muscles in cases of "so-called concomitant strabismus."

Dr. Anderson's criterion for operative treatment is the disability resulting from an ocular palsy rather than the paresis itself, and he advises careful consideration of the possibility of spontaneous recovery. Although he does not attempt to describe the technique of orthoptic training, he suggests that it has an important position in the treatment of the majority of ocular palsies. He also gives concise accounts of various diagnostic tests (including a simplified routine for those not equipped with a Hess or projection apparatus) and short discussions of operative procedures.

P. W.

Recent Advances in Medicine: Clinical, Laboratory, Therapeutic

G. E. Beaumont & E. C. Dodds. Twelfth edition. London, J. & A. Churchill Ltd., 1947. xii + 422 pages; 42 illustrations. 21 × 14 cm. £1 1s. [£1.05]

In this 12th edition of the *doyen* of the famous series, the authors have once again justified the title. The chapter on chemotherapy has been rewritten and a new section added on synthetic antimalarial drugs. A new chapter has been added on the antibiotic substances, discussed both from the clinical and laboratory aspects. The chapter on vitamins has been considerably altered; in particular the sections on the vitamin B complex and vitamin K have been rewritten, and notes have been included on biotin, folic acid and dicoumarol. New articles deal with thiouracil, primary atypical pneumonia, infective hepatitis, homologous serum jaundice, bone marrow transfusion, the use of thiocyanates in the treatment of high blood pressure and the treatment of malignant disease by synthetic oestrogens. Chapter XIV, Blood and Urine Analysis, has been revised to include the latest procedures.

Unfortunately, in order to preserve the size of the volume certain sections, such as those dealing with the kidneys and diphtheria, have had to be omitted. However, such pruning is inevitable in a book of this kind if it is to retain one of its most useful features, namely ease of handling.

G. J. H.

A Handbook of Midwifery for Pupil-Midwives, Midwives, and Obstetric Dressers

Comyns Berkeley. Thirteenth edition. London, Cassell & Company Ltd., 1946. ix + 456 pages; 88 illustrations. 19 × 12 cm. 12s. 6d. [£0.625]

Since 1906, this book, a standard work of its class, has passed through thirteen editions and twelve reprintings. While the book caters for the needs of those preparing for the examinations of the Central Midwives Board (for example, the chapter on hormones is in the present edition transferred to an appendix, as a result of the C.M.B. notification to examiners that pupil midwives need not be examined in this subject), it fulfils a wider function than that of an examination text. Authoritative answers are given to a wide range of problems, but, at the same time, clear and concise reasons are given for the validity of the answers.

The sections on treatment of unavoidable haemorrhage and on blood transfusion have been rewritten and a brief note on the Rh factor has been added.

A clear and full index adds to the value of the book.

P. W.

Lunacy and Mental Deficiency. The Thirty-third Annual Report of the Board of Control for the Year 1946. Part I.

Board of Control. London, His Majesty's Stationery Office, 1947. 40 pages. 24 × 15 cm. 9d. [£0.0375]

Because of the changes which will result from the operation of the National Health Service which came into force in July 1948, this report is the last to be presented to Parliament in this form. The Board's administrative functions have now been transferred to the Ministry of Health.

The number of persons under care in 1946 was 146,444 and there were 6,009 more admissions during the year than in 1945. There has been a steady rise for several years in the number of admissions. Voluntary admissions (18,059) compare with 9,651 in 1938, and follow the development in both doctor and layman of a much greater awareness of the importance of early treatment.

There is an aggregate overcrowding rate of 13.1%; 15,170 beds were not available (10,417 being still diverted to wartime services, 3,080 unoccupied owing to shortage of staff, and 1,673 awaiting restoration or re-equipment). One of the most serious shortages is that of female nurses, but a slight improvement is evident in some hospitals.

It is a matter for satisfaction that, in the treatment of mental disorders, some form of physical treatment is used in every mental hospital to supplement psychotherapy and other methods. With regard to prefrontal leucotomy, some time must elapse before opinion can crystallize as to the efficacy of this form of treatment, but there is reason to hope that this operation offers a probability of relief and the possibility of recovery.

Emphasis is laid on the importance of occupational treatment for chronic patients. The shortage of social workers trained to undertake work in mental health is acute and the report suggests the need for a special course for training social workers for mental-deficiency services.

L. T. M.

Diseases of the Nervous System

W. Russell Brain. Third edition. London, Geoffrey Cumberlege, Oxford University Press, 1947. xx + 987 pages; 80 illustrations. 22 × 14 cm. £1 17s. 6d. [£1.875]

During the fourteen years that have elapsed since the 1st edition of this book, it has earned for itself

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BOOK REVIEWS

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[1229] The Secret Instrument (The Birth of the Midwifery Forceps)

Walter Radcliffe. London, William Heinemann (Medical Books) Ltd., 1947. xvi + 83 pages; 23 illustrations. 19 x 13 cm. 10s. 6d. [£0.525]

(i) Prologue; (ii) mediaeval midwifery; (iii) the Chamberlen family; (iv) Hugh Chamberlen's secret; (v) the Dutch mystery; (vi) three Essex doctors; (vii) Mr. Smellie and Doctor "Slop"; (viii) the years of invention; (ix) the vectis. Bibliography. Appendix. Index.

[1230] The Story of St. Thomas's 1106-1947

Charles Graves. London, Faber and Faber Ltd., for St. Thomas's Hospital, 1947. 72 pages; 41 illustrations; 8 plates. 24 x 16 cm. 8s. 6d. [£0.425]

(i) The religious foundation 1106–1540; (ii) the Royal Hospital 1553–1700; (iii) the early school of medicine 1700–1871; (iv) the birth of modern nursing 1871–1939; (v) the war and after 1940–1947.

[1231] The Fever Bark Tree. The Pageant of Quinine

M. L. Duran-Reynals. London, W. H. Allen, 1947. 251 pages. 19 x 13 cm. 8s. 6d. [£0.425]

(i) Of fevers; (ii) the countess's powder; (iii) the Jesuits' powder; (iv) philosophical interlude; (v) the wonderful secret of the Englishman; (vi) the fever bark tree; (vii) the Botanical Institute of the New Kingdom of Granada; (viii) the breaking of the spell; (ix) scientific interlude; (x) poor man's quinine; (xi) the betrayal; (xii) rich man's quinine; (xiii) Hercules, the hydra, and the birds; (xiv) Bataan and Corregidor; (xv) of fevers.

[1232] The Medical Writings of Anonymus Londinensis

W. H. S. Jones. Cambridge, Cambridge University Press, 1947. viii + 168 pages. 22 x 14 cm. 12s. 6d. [£0.625]

(i) Anonymi Londinensis Iatrica; (ii) Excursus I. The nature of Greek thought. II. The nature of Greek medicine. Index of *Notabilia.*

a position as the standard english work on neurology. Owing to the fact that seven war-years have passed since the 2nd edition, much revision has been necessary. The lessons of war have been no less in the neurological field than in others. New light has been thrown upon the nature of peripheral-nerve injuries and has entailed the rewriting of the relevant section. A new chapter is devoted to the nutritional disorders of the nervous system, based upon the unfortunate cases found in prisoner-of-war camps. Herniated lumbar intervertebral disk now occupies most of the space formerly devoted to sciatic neuritis. New sections have been added on equine encephalitis, myelopathy, the nervous complications of epidemic hepatitis, spinal radiculitis, and platybasia. The section on the psychological aspects of neurology has been recast and now includes the status of psychogenic symptoms, psychotherapy and psychometric tests. Like its predecessors, this edition is well supplied with illustrations and references, and the whole production is well up to the standard expected from this publisher.

G. J. H.

Ulcer of the Stomach, Duodenum and Jejunum

Ralph C. Brown. New York, Oxford University Press; London, Geoffrey Cumberlege, 1946. iv + 104 pages; illustrations. 24 × 16 cm. 12s. 6d. [£0.625]

This book, reprinted from the Oxford Loose-Leaf Medicine, with pages similarly numbered, is a general review, on the lines of a text-book, of ulcer of the stomach, duodenum and jejunum. Sections are devoted to etiology, pathogenesis, morbid anatomy, symptoms, diagnosis and treatment. Gastric and duodenal ulcer are not clearly separated and often are dealt with together as peptic ulcer. Otherwise the statements are in general accord with the views held at the present time. A few cases are quoted briefly from the author's personal experience, and there are a few brief references to research by others. No new ground is broken. The figures, with the exception of the frontispiece, are contour-drawings from radiographs and illustrate clearly the well-known features of peptic ulcer.

Henry Tidy

Traumatología Ocular de Urgencia

José Casanovas. Barcelona, Ediciones BYP, 1947. (Colección Española de Monografías Médicas, Volume 67-68.) 147 pages; 20 illustrations. 20 × 14 cm.

Dr. Casanovas, who is a member of the Faculty of Medicine in Barcelona, has written this short book to help medical men who are not specialists in ophthalmology but who may be required to give emergency treatment for eye injuries. The author begins by describing methods and apparatus for the examination of the eyes and for the location of injuries and foreign bodies in the eyes. Further chapters describe various eye injuries and their treatment. This book also includes Vol. 67-68 of the *Colección española de monografías médicas*, containing two original papers and reprints of five articles originally published in other journals.

V. E. C. M.

Symptoms and Signs in Clinical Medicine: an Introduction to Medical Diagnosis

E. Noble Chamberlain. Fourth edition. Bristol, John Wright & Sons Ltd., 1947. vii + 463 pages; 346 figures. 23 × 15 cm. £1 10s. [£1.5]

We welcome the 4th edition of this book, which first appeared in 1936, and which is very widely used by medical students beginning their work in the wards. Dr. Noble Chamberlain surveys a vast ground in this introduction to medical diagnosis. The main chapters of the book cover the clinical examination of the patient and the methods of taking a history and of eliciting physical signs, and briefly discuss the differential diagnosis of the abnormal signs. This part provides a clear account of the basic essentials of clinical medicine. The later chapters of the book, which deal with subsidiary methods of investigation, medical operations, radiology and clinical pathology, bear little relation to the title, are too condensed and lacking in detail for the enquiring student, and are more open to criticism. The directions for some of the operations, such as bronchography, while given in some detail, are in fact incomplete. Fig. 287, showing a black-coated doctor performing a lumbar puncture on a sitting patient, watched by an unmasked attendant, should surely be excluded from an introductory volume for the student; and lipiodol is now rarely, if ever, used intrathecally in the localization of spinal tumours.

It seems a pity that these chapters take up space which might profitably be filled by an expansion of the earlier part of the book. A fuller dicussion of the causation of some of the physical signs would be of great value, and several sections require revision. A more complete account is needed of the eye signs in thyrotoxicosis, distinguishing clearly between exophthalmos and lid retraction; the section on the diagnosis of diseases of the liver is inadequate (and infective hepatitis is not mentioned as a cause of hepatic enlargement); and a coloured plate of the common skin rashes should surely appear in a volume devoted to physical signs. Since the introduction of chemotherapy, the student will rarely see a case of lobar pneumonia in which the "fever and constitutional signs continue . . . for a week, and the pyrexia then subsides by crisis", and he will find it difficult to appreciate how alkalis, by causing relaxation of the hypertonic stomach wall, can lead to a correct adaptation between the stomach and its contents, with the relief of gastric pain.

It might, at first sight, appear invidious to criticize a work which, by its popularity, has proved that it fills a need, but the more widely used a textbook, the more important it is that it should be as free from fault as possible.

M. L. Rosenheim

The Sanitary Inspector's Handbook: A Manual for Sanitary Inspectors and other Public Health Officers

Henry H. Clay. Sixth edition. London, H. K. Lewis & Co. Ltd., 1947. xxii + 545 pages; 99 illustrations. 22 × 14 cm. £1 2s. [£1.1]

The range of knowledge required by modern sanitary inspectors is very wide and this book provides an excellent guide to the many facets of their work. The great increase in legislation and regulations dealing with public health, as well as the advances in the technology of hygiene and sanitation that have taken place since the previous edition, has entailed a thorough revision and the addition of a considerable amount of new material. This book serves two valuable purposes: it is the essential textbook for the prospective sanitary inspector and an invaluable work of reference in public health departments. The illustrations, many of which have been redrawn in this edition, are models of clarity and should be of much use to the student.

G. J. H.

A Way of Life for the Handicapped Child: a New Approach to Cerebral Palsy

Eirene Collis. London, Faber & Faber Ltd., 1947. 183 pages; illustrations. 21 × 14 cm. 10s. 6d. [£0.525]

The handicapped child of this book is the victim of cerebral palsy; the author studied under Dr. W. M. Phelps in the USA and is the pioneer in Great Britain of his approach in the treatment of such children. The London County Council gave her every facility to carry out the treatment in one of their children's hospitals and this book embodies the results of a personal study of individual children over a four-year period. The opening chapters deal with etiology, types, signs and symptoms of cerebral palsy and the psychology of the child so afflicted. It is assumed that treatment should consist in training a different part of the brain to take over the function of the damaged areas and subsequent chapters deal with the control of specific movement, e.g. strengthening the abdominal and respiratory muscles, proceeding to voluntary attempts at head raising, correct sitting and trunk movements, and occupational therapy in which the application of trained movements to specific skill is stressed. It includes the activities of the normal child, such as sand games, playing with blocks, buttoning and unbuttoning, etc. There are many illustrations of mechanical aids and supports, such as chairs, tables and sliding boards, made to the author's own designs, together with examination charts and descriptions of physical exercises, with their accompanying music, for routine work.

The book concludes with an excellent summary of this new approach, emphasizing that children with cerebral palsy are not necessarily mentally defective and that, while there is as yet no known cure for the condition, with patience and understanding on the part of the therapist they may be trained to become normal and happy members of the community.

D. F. A.

Health the Unknown: the Story of the Peckham Experiment

John Comerford. London, Hamish Hamilton, 1947. 144 pages. 19 × 13 cm. 7s. 6d. [£0.375]

Mr. Comerford tells in his preface how he read *The Peckham experiment* by Pearse & Crocker and resolved to write a simplified and shortened version for the non-scientific reader; his success has been uneven. Here and there unexplained scientific terms appear, simple popular "journalese" alternates with polysyllabic passages and there are a good many intrusions of pseudo-philosophy, but on the whole the idea and the spirit of the Peckham Pioneer Health Centre are well caught and vividly if impressionistically presented. The book bubbles with uncritical enthusiasm which will irritate the scientific reader but is likely to achieve the author's intention of arousing the interest of the ordinary man and leading him on to further study of the subject.

Too often the opinions of the staff of the Centre are quoted as if they were the dogmatic statements of accepted authorities and there are places in which Mr. Comerford implies that the Centre itself is a final solution to social problems rather than a laboratory in which they can be studied, a claim which the staff themselves are wisely reluctant to make. Again, the author's sadly imperfect knowledge of british public-health and social-service work betrays him into belittling its actual success and its potentialities. Read with caution the book has real value but, unfortunately, it is designed to appeal to the less cautious class of reader.

John D Kershaw

Man and Animals: What They Eat and Why (A Manual of Nutrition)

Ben Dawes. London, Longmans, Green & Co., 1947. vii + 100 pages. 19 × 13 cm. 7s. 6d. [£0.375]

This is not, as might be imagined from the title, a work of a popular nature; for the author, Reader in Zoology at King's College, London, presupposes in the lay reader, for whom it is intended, a knowledge of chemistry and physics in relation to biology. It is an amplified excerpt from a projected large general work on animal biology and deals with the fundamental chemical and physical relations between the living animal and the food it eats. The subject-matter is divided into three sections, on protoplasm, on the nature of food, and on the uses of food. The author would seem to be somewhat over-optimistic in thinking that lay readers will have the patience and intelligence to master the necessary use of scientific terms and in hoping that it will serve "to increase an instructed public interest in the problem of why we eat what we do." It should however prove of value to students of biology, zoology and biochemistry and to research workers in the field of animal nutrition.

G. J. H.

A Textbook of Dietetics

L. S. P. Davidson & Ian A. Anderson. Second edition. London, Hamish Hamilton Medical Books, 1947. xix + 517 pages; illustrated. 22 × 14 cm. £1 1s. [£1.05]

This book is directed mainly to the student and to the general practitioner and deals with the subject under three main headings: the physiology of nutrition, diet in periods of physiological stress, and dietetic treatment in established disease. The war-years have seen great developments in each of these branches and the modification of the text to include them has involved a not inconsiderable increase in its length.

In the section on the physiology of nutrition, the chapters on proteins and vitamins have needed the most revision; the former now includes an account of protein hydrolysates and the latter a discussion of the use of folic acid in macrocytic anaemia. In the second section a new chapter has been added on the treatment of starvation, a subject that came into prominence with the liberation of prisoners from the concentration and prisoner-of-war camps. A useful new chapter is the one on special feeding methods, which are dealt with in some detail. The section on the treatment of established diseases has been brought up to date by new articles on the use of globin insulin, on the dietetic treatment of peptic ulcer and on other topics. The final section which deals with tables, recipes and diet sheets, has been completely redrafted in the light of the most recent authoritative official figures. It also includes a new chapter on methods of carrying out dietetic surveys.

G. J. H.

Essentials for Final Examinations in Medicine

John de Swiet. Third edition. London J. & A. Churchill Ltd., 1947. vi + 178 pages 19 × 12 cm. 9s. [£0.45]

This book, as the author explains in the preface to the 1st edition, is intended to aid the student in his last revision for "finals", and not to replace the standard text-books of medicine. It can only summarize for him the knowledge he should already have gained from them. In this edition new material has been introduced on penicillin, pellagra and related disorders, osteo-arthritis, chronic subdural haematoma and primary atypical pneumonia. An index has been added.

H. C.

Food Poisoning: its Nature, History and Causation. Measures for its Prevention and Control

Elliot B. Dewberry. Second edition. London, Leonard Hill Ltd., 1947. xii + 246 pages; 58 illustrations. 22 × 14 cm. 17s. 6d. [£0.875]

Although the author of this book claims no originality for it, the 1st edition filled a gap in medical literature by presenting in one volume the fundamental facts relative to many kinds of food poisoning. Previously, in order to acquire this information an extensive search of many different sources was necessary. For those wishing to read more widely on any topic an extensive bibliography is appended to each chapter. This edition has been brought up to date by the addition of new material, including a chapter on staphylococcus food-poisoning, a type of illness which has been much to the fore in recent years. Interest is added to the text by photographs of some of the early investigators in this field. It is a pity, however, that the modern practice of carrying the illustrations to the edge of the page has been adopted, as this inevitably leads to their suffering damage under the extensive use that a work of this type is likely to get.

G. J. H.

Propedéutica de Patología Circulatoria en las Profesiones

Domingo de Durán Arrom. Madrid, Ediciones Morata, 1947. 171 pages; 28 illustrations. 25 × 18 cm. 40 ptas.

Dr. Durán Arrom has published many works on cardiological subjects, of which he has made a special study. He here describes disorders of the heart and circulation caused by trauma, occupational diseases, or infection. He discusses preventive measures and questions of diagnosis, treatment and medico-social care. The book is clearly and simply written and well illustrated, and contains useful author- and subject-indexes.

V. E. C. M.

Vital Statistics and Public Health Work in the Tropics, Including Supplement on the Genealogy of Vital Statistics

P. Granville Edge. London, Baillière, Tindall & Cox, 1947. xii + 268 pages. 22 × 14 cm. 15s. [£0.75]

The 2nd edition of this work consists of a 2nd impression of the original edition, complete with index, and with about 80 additional pages entitled "The genealogy of vital statistics". To those who have not yet seen the 1st edition of 1944 the reprint will be of value. It is primarily addressed to those interested in british tropical territories, but will be helpful to all who have to deal with problems of vital statistics in the tropics.

The new historical section, with its separate index, breaks new ground. It is not confined to the tropics, and sketches the whole development of vital statistics from the Babylonian to the British Empire. The author certainly succeeds in his purpose of showing that this science is "the lineal descendant of a really ancient family", but he does not attempt to relate its history to the social and economic conditions that produced it. The study is of necessity only a summary, and will provide the medical historian with much interesting material and many references.

D. T. Richnell

Child Health and Development by Various Authors

Edited by *Richard W. B. Ellis.* London, J. & A. Churchill Ltd., 1947. viii + 364 pages; 49 illustrations. 22 × 14 cm. 18s. [£0.9]

Professor Ellis is to be congratulated on the panel of eminent specialists who have contributed to this symposium. The book is intended to counterbalance the "too-exclusive preoccupation with disease in childhood" during medical training, by emphasizing the importance of child health. It is anticipated that it will be of value also in the training of nurses, health visitors and social workers.

The book is divided into two parts: the first deals with the physical, emotional and intellectual development of the normal child, and the second with various social services and conditions relating to child health. The section on development covers various aspects from the ante-natal period to puberty, including antenatal and postnatal care, the development of the foetus, nutrition and feeding, the teeth, growth, intellectual and emotional development, and immunity. The section on social aspects covers genetics, mortality, infant welfare, school health-services, nursery schools, the educational system the care of the homeless, and juvenile courts. One appendix presents an exposition of blood groups and the rhesus series, while another gives a useful annotated list of voluntary organizations concerned with child health. The whole symposium very adequately fills a gap in medical literature and should prove a valuable handbook for doctors, nurses and lay workers.

G. J. H.

Tuberculosis and Chest Disease for Nurses

G. S. Erwin. London, J. & A. Churchill Ltd., 1946. vii + 236 pages; 39 illustrations. 21 × 14 cm. 10s. 6d. [£0.525]

The title of this book by the Medical Superintendent of the Liverpool Sanatorium, Frodsham, must be read in its literal sense. It is designed to explain in suitable terms the etiology, pathology, diagnosis (both clinical and laboratory), treatment and complications of tuberculosis and of non-tubercular pulmonary disease. It is not a textbook of the nursing technique proper to these conditions but a book which aims at giving the nurse a better theoretical understanding of them, both to increase her own efficiency and to fit her to undertake the work of "a health educator and teacher".

Rather more than half the book is devoted to pulmonary tuberculosis. This section, in addition to the consideration of pulmonary tuberculosis as a disease, gives one chapter to the discussion of various factors such as marriage, pregnancy, age, inheritance and co-existent physical and mental disorders, in relation to pulmonary tuberculosis; a second to a review of the home and institutional managements of the disease; and a third to the public-health aspects of tuberculosis. This last chapter ends with a brief note on the control of tuberculosis amongst nurses themselves.

Part II of the book deals briefly with non-pulmonary tuberculosis and its treatment, medical, surgical and orthopaedic, while part III is devoted to non-tuberculous pulmonary disease. In a short appendix the causes of haemoptysis and of pleural effusion are listed.

P. W.

A Guide to Anatomy for Students of Physiotherapy and Electro-therapy, etc.

E. D. Ewart. Sixth edition. London, H. K. Lewis & Co. Ltd., 1947. xii + 318 pages; 119 illustrations. 22 × 14 cm. £1 5s. [£1.25]

This work, of which the 5th edition was published in 1943, first appeared in 1921, with the express intention of providing a handbook for students preparing for examinations in medical gymnastics and massage. Consideration of body-structures is therefore limited by the special needs of that section of students to which the book is addressed.

It is divided into five sections: osteology, the trunk, head and neck, upper limb and lower limb. The last four sections are preceded by a short introductory chapter in which the general structure of body parts is considered, and each section ends with notes on surface markings.

The new nomenclature has been introduced in this edition, and the illustrations, with which the book is generously provided, have been largely revised.

An appendix gives anatomical questions recently set in the examinations of the Chartered Society of Physiotherapy, of the Association of Occupational Therapists and of the Society of Radiographers. The book is attractively laid out and has a useful index.

P. W.

Gardiner's Handbook of Skin Diseases

[*F.*] *Gardiner.* Fifth edition revised by John Kinnear. Edinburgh, E. & S. Livingstone Ltd., 1948. xv + 250 pages; 80 figures; 20 plates. 19 × 13 cm. 15s. [£0.75]

This useful little book is intended as a handbook for students, general practitioners and nurses and, as such, attempts to deal adequately with the common skin diseases and briefly with the rarer ones. The long interval since the appearance of the previous edition in 1939 has made extensive revision necessary and the whole book has been brought up to date in the light of recent advances, particularly on the therapeutic side. It now includes the most modern methods of treatment, such as BAL in exfoliative dermatitis, penicillin in staphylococcal infections, and sulphapyridine in dermatitis herpetiformis. The illustrations, in particular the coloured plates, are extremely good and are in keeping with the general quality of the production.

G. J. H.

Current Therapies of Personality Disorders: the Proceedings of the Thirty-fourth Annual Meeting of the American Psychopathological Association, held in New York City, April, 1945

Edited by *Bernard Glueck.* London, William Heinemann Medical Books Ltd., 1946. 296 pages. 24 × 16 cm. 17s. 6d. [£0.875]

It was a happy idea to publish these Proceedings of the American Psychopathological Association. The Presidential Address contains some thought-provoking quotations, including one from the undelivered last speech of the late President Roosevelt: "Today we are faced with the pre-eminent fact that if civilization is to survive, we must cultivate the science of human relationships" . . . which last phrase, Dr. Glueck suggests, might be regarded as being particularly addressed to psychiatrists.

There is an interesting paper by Elsie B. Kris on the use of electro-shock therapy at the Pilgrim State Hospital. She starts her treatment with a rather higher voltage (90-100 volts) than that used in Britain but finds like the British that a much higher voltage is rarely necessary. Her statement that "Patients with marked hypertension have been found to stand a full course of treatment without any kind of embarrassment" is surprising, as patients with hypertension are regarded as unsuitable for this form of therapy by some doctors. This paper should be read in conjunction with two others: Pharmacological Therapies in Psychiatric Practice, and Public Health Aspects of Insulin and Other Shock Therapies. The three together form a useful review of the development and practice of shock therapy.

Many will agree with Professor T. V. Moore that in dealing with the problem child: "It is not necessary to scold and condemn in order to alter conduct. One waits and leads. There is no necessity of giving advice when advice will not be accepted." His attempts to develop the character of adolescents through the reading of suitable books should command attention. He claims that his treatment is of special value in the behaviour disorders of preadolescent and adolescent children.

Like most works of a composite character not all the papers have the same value, but most of them will repay careful reading and the whole work reflects a refreshingly practical outlook.

F. T.

Pharmacology and Therapeutics

Originally written by *Arthur R. Cushny.* 13th edition by *Arthur Grollman* & *Donald Slaughter.* London, J. & A. Churchill Ltd., 1947. 868 pages; 74 illustrations. 23 × 14 cm. £2 5s. [£2.25]

Since the last edition of this book in 1940, one of the two former editors has died and the other resigned, so that this edition is in new hands. The new editors have had therefore the difficult task of incorporating the changes necessitated by the notable advances in this subject during the last seven years, and of preserving the character of the original work. They appear to have been successful in both aspects. The bias of this book is in favour of practical therapeutics, so some of the older material of a more experimental nature has been omitted from this edition. It is intended as a textbook rather than a compendium of pharmacological knowledge. Although an american work, it caters for the british reader by giving the british nomenclature as well as the american, in cases where practice in the two countries differs; it also lists *British Pharmacopoeia* preparations as well as those of *The Pharmacopeia of the United States.* References are confined to those of a pioneer nature and to those which themselves include extensive bibliographies.

G. J. H.

Hey Groves' Synopsis of Surgery

Edited by *Cecil P. G. Wakeley.* Thirteenth edition. Bristol, John Wright & Sons Ltd., 1947. viii + 637 pages. 19 × 13 cm. £1 5s. [£1.25]

During the 40 years that have elapsed since the first appearance of this book, many thousands of students must have carried it about with them in the wards and out-patient departments, as did the present editor, Sir Cecil Wakeley. The concise manner in which the whole range of surgical knowledge is presented is the key to its popularity, which has been sustained by the constant revision to which it has been subjected in each edition. Since the previous edition, two years have passed in which advances have been made in many branches of surgery, and this edition has been thoroughly revised to include them. The sulphonamide group of drugs and penicillin now play a large part in surgical treatment; they are covered in this book not only in the sections dealing with the treatment of acute infections but also in a new chapter on chemotherapy. The numerous line-drawings add to its value as a teaching instrument, and the excellent index makes quick reference an easy matter.

G. J. H.

Diseases of the Nose, Throat and Ear. A Handbook for Students and Practitioners

I. Simson Hall. Fourth edition. Edinburgh, E. & S. Livingstone Ltd., 1948. xii + 463 pages; 82 figures; 8 plates. 19 × 12 cm. 15s. [£0.75]

The format of the 4th edition of this useful guide remains essentially the same as that of the last one, in 1944. The most outstanding advances in otology of recent years are discussed, among them the use of the fenestration operation in otosclerosis, and the author has incorporated alterations in treatment that have become general since the introduction of penicillin.

H. C.

Experimental Physiology for Medical Students

D. T. Harris. Fourth edition. London, J. & A. Churchill Ltd., 1947. xi + 299 pages; 257 figures; 1 plate. 26 × 16 cm. 18s. [£0.9]

The divergent techniques available for the performance of many laboratory exercises, and the fact that teachers tend to emphasize different aspects of the subject, do not facilitate the preparation of a generally satisfactory textbook of experimental physiology. Professor Harris has made a praiseworthy effort to cope with these difficulties in the 4th edition of his *Experimental physiology*, which sets forth clearly and concisely the usual class exercises for students for the second M.B. examination, with enough scope in methods and sufficient detail in description to satisfy the requirements of all laboratories. The exercises amply fulfil the needs of M.B. students or of students working for a pass B.Sc. degree, although too advanced for a conjoint student and just falling short of the requirements of the Honours B.Sc. student. Professor Harris' book shows clearly the effect of the trend, now operative over twenty years, to include mammalian and especially human experiments. Many of these are necessarily demonstrations. The electronic devices and schematic presentation of circuits may not be as intelligible to the present-day students as Professor Harris believes, but they serve the useful purpose of focussing attention on the practical advantages of such understanding. This textbook is a most valuable asset to any physiological laboratory.

E. F. McCarthy

Insect Pests

W. Clunie Harvey & *Harry Hill.* Second edition. London, H. K. Lewis & Co. Ltd., 1947. xi + 347 pages; 27 figures. 19 × 13 cm. 14s. [£0.7]

This handbook was presumably written for the assistance of sanitary inspectors and other health officials of local authority health-departments. The authors have clearly had much experience in control of domestic insect pests and they give much sound advice on practical procedure and legal responsibility.

This new edition includes a fairly long section containing useful information about the new insecticide DDT. There is also a shorter account of "Gammexane", but this is ambiguous, for it overlooks the importance of basing recommendations on the *gamma* isomer content. There are some rather unnecessarily full sections on insecticides which have become more or less obsolete or undesirable, especially fumigants such as ortho-dichlorbenzene, heavy naphtha, and formalin.

The biological data are somewhat less satisfactory than the portions devoted to control methods and procedure. Most of the text-figures are very poor and provide little help in identification of the pests. Since the authors consider the scientific names of the insects to be worth including, they would have done well to check the spelling of several of them.

A new chapter is given in this edition devoted (somewhat incongruously) to "mosquitoes and moths" (i.e. clothes moths). This addition should be useful, since local health-departments often receive queries and complaints about these insects.

J. R. Busvine

Practical Physiological Chemistry

Philip B. Hawk, Bernard L. Oser & William H. Summerson. Twelfth edition. London, J. & A. Churchill Ltd., 1947. xiv + 1323 pages; 329 figures; 5 plates. 23 × 15 cm. £2 10s. [£2.5]

This, the oldest of the american textbooks of physiological chemistry, was first published in 1907; the 11th edition appeared in 1937. Dr. Oser is now a co-author with Dr. Hawk; the third collaborator, Professor Summerson, is associate professor of biochemistry, Cornell University Medical College.

This edition has been largely rewritten and in spite of the exclusion of methods now obsolete or of minor importance, the inclusion of new matter has increased the bulk of the book by approximately a third. This new matter, to quote the preface, includes sections ". . . on the polarograph; on isotopes; on the sulfa drugs; on metabolic antagonists and antibiotics; on the Warburg tissue-slice procedure; on the theory and practice of photometric analysis; on the electrophoretic fractionation of the plasma proteins; on the composition of foods; and on the various vitamins whose importance has become recognized since the last edition . . ."

P. W.

Biology for Medical Students

C. C. Hentschel & W. R. Ivimey Cook. Fourth edition. London, Longmans, Green & Co., 1947. xii + 752 pages; 453 illustrations. 22 × 14 cm. £1 5s. [£1.25]

This is the 4th edition of a book which first appeared in 1932 and which has seen two new impressions of its 1st edition, two of its 2nd and three of its 3rd. Revision was deferred until the present edition, that is until the new form of the teaching of biology for medical students was settled. As the type for the book was completely destroyed in 1945, the illustrations have had to be redrawn.

The botanical chapters have been entirely rewritten, more space being devoted to plant physiology. Whilst less alteration was needed in those on zoology, a new chapter on bionomics has been included. In the view of the authors the alterations are so extensive that the new edition should be regarded as substantially a new book.

J. L.-J.

Textbook of Histology for Medical Students

Evelyn E. Hewer. Fourth edition. London, William Heinemann Medical Books Ltd., 1947. viii + 407 pages; 393 figures. 24 × 17 cm. £1 1s. [£1.05]

The 3rd edition of this standard textbook of histology was reviewed in the *British Medical Bulletin*, 1944, 2, 129 (*BMB* 387/35). In the new edition a 3-page chapter has been added on the protective mechanism of the body: this lists the usual sources of entry of injurious substances into the body, the structures preventing such entry, and the methods by which the body deals with infection or damage to tissues. The author has also enlarged the sections on the reproductive organs and on the respiratory system.

The illustrations are black-and-white photomicrographs and semi-diagrammatic line-drawings. New photomicrographs have been added, and material of academic rather than practical interest deleted, so that the volume has been increased by only about 40 pages.

This textbook covers elementary histology for medical students; references to further work are sparse and lack details.

H. P.

Food Inspection Notes : a Handbook for Students

H. Hill & E. Dodsworth. Second edition. London, H. K. Lewis & Co. Ltd., 1947. vii + 125 pages. 17 × 11 cm. 6s. [£0.3]

This small handbook, the 1st edition of which appeared in 1943, is prepared by two sanitary inspectors with the purpose of presenting in summarized form present-day knowledge of foods and their inspection, to meet the needs of public-health officials and students. The text of the new edition has been revised, amended where necessary and brought completely up to date. Although the legal aspects of the subject are not dealt with, the book should prove, within its limitations, especially useful to students preparing for examinations.

W. W. S.

Illustrations of Regional Anatomy

E. B. Jamieson. Seventh edition. Edinburgh, E. & S. Livingstone Ltd., 1947. 320 plates. 21 × 16 cm. (In seven separate sections.) £3 15s. [£3.75]

These illustrations are based on the work of Dr. Jamieson as Demonstrator in the Anatomy Department of Edinburgh University. They were originally diagrams used to illustrate his lectures on regional anatomy, collected and published in book form at the request of undergraduates. Some of the figures are copies of blackboard diagrams, but most of them are the result of observation of actual specimens. In this new edition, in one plate, the original drawing has been altered; in others, alterations, generally in colour, have been made and pointer-legends have been corrected. Explanatory additions have been made in some of the foot-legends of the figures.

H. C.

The Midwife's Text-Book of the Principles and Practice of Midwifery

R. W. Johnstone. Third edition. London, Adam & Charles Black, 1947. viii + 398 pages; 205 illustrations. 22 × 14 cm. 18s. [£0.9]

Clarity, readability and a high standard of illustration are the hallmarks of this book, of which the 1st edition appeared in 1944 and the 2nd in 1946. There has been a general revision of the text for this edition, and a discussion of nitrous oxide and air analgesia has been added to the chapter devoted to drugs and solutions in common use. A new chapter on the Rh factor and its importance in midwifery has been included.

P. W.

Supplement to the Catalogue of Lewis's Medical, Scientific and Technical Lending Library: Including a Classified Index of Subjects with the Names of those Authors who have Treated Upon Them. Supplement, 1944-1946

H. K. Lewis. London, Lewis's Library, 1947. iv + 175 pages. 22 × 14 cm. 5s. [£0.25] (To subscribers to the library, 2s. 6d.)

The present supplement is a useful guide to recent accessions to Lewis's Library, and to readers abroad will form an invaluable reference work to medical and scientific books published in Britain and the USA during 1944-46. American volumes are easily identified, as places of publication have been included; moreover, the prices of british works are quoted in sterling. No other single publication contains the same information, and books can be traced otherwise only by tedious search through such serial publications as the *Quarterly Cumulative Index Medicus* book lists or the technical books supplements issued with *Nature*.

F. T.

An Introduction to Gastro-Enterology. A Clinical Study of the Structure and Functions of the Human Alimentary Tube

James Dunlop Lickley. Bristol, John Wright & Sons Ltd., 1947. viii + 143 pages; 21 illustrations. 19 × 13 cm. 8s. 6d. [£0.425]

This work is, from its length, obviously intended only as a general reminder of some of the problems involved in diagnosis and treatment of gastro-intestinal disorders. It is addressed to senior medical students, younger physicians and medical men returning from the armed forces. It is divided into four parts, on structure, function, abnormal conditions, and practical clinical applications.

D. T. Richnell

Praktikum der Physiologischen Chemie

H. Lieb. Graz, Jos. A. Kienreich, 1946. 215 pages; 19 figures. 20 × 14 cm.

The author is the Director of the Medico-Chemical Institute of the University of Graz. The book is based on lectures accompanying practical exercises at the Institute and is intended primarily for students. The author has, however, expanded the book by the inclusion of several clinical methods of analysis in the hope that it may also be of use to doctors engaged in clinical work. Each chapter consists of short general remarks on the chemical nature of the substances to be tested, followed by a simple and lucid description of the tests themselves. The more important quantitative methods of analysis are given in an appendix.

W. M. G.

Nothing New Under the Sun

J. P. Lockhart-Mummery. London, Andrew Melrose Ltd. [1947] x + 178 pages; illustrations. 22 × 14 cm. 12s. 6d. [£0.625]

The contents of this book, which consists of a collection of essays, are aptly summed up by its title and by the Herrick quotation at the beginning of the preface—"Nothing is new; we walk where others went." In many of his essays, which have arresting titles, the author demonstrates that man, being an essentially imitative animal, has observed and exploited the phenomena of Nature for his own purposes.

The essays are not confined solely to medical subjects, but diverge widely, ranging from an account of the skill in the art of advertisement exhibited in the animal and vegetable kingdoms in relation to our own familiar commercial boostings, to a description of the force of the eruption of Krakatoa, as compared with the too well-known atomic-bomb explosions in Hiroshima, Nagasaki and the Bikini Atoll.

Such subjects as abnormalities of growth, diet and allergy are encountered in essays of medical interest. There are also references to quacks and charlatans, among them being Cagliostro, and Graham of the "celestial bed" fame. History is represented by, amongst other things, a description of water-supply through the ages, and an account of the development of architecture, from primitive hut-dwellings to the use of ferro-concrete and steel girders in modern building construction. The last essay, called Science on Trial, is an attempt to assess dispassionately the effect of man's application of scientific discovery, with its potentialities for good and evil, on economic and social structure of the past, present and future.

Nothing new under the sun is written throughout in a simple, unconventional style, and as the author says in the preface, is intended to afford interest and amusement to its readers, whose enjoyment will no doubt be increased by William Wood's delightful illustrations.

S. M. S

Spanish-English Medical Dictionary

Maurice McElligott. London, H. K. Lewis & Co. Ltd., 1946. viii + 250 pages. 17 × 11 cm. 12s. 6d. [£0.625]

It is apparent that the compiler of this small dictionary has taken considerable trouble to ensure the accuracy of the 14,000 spanish words listed and their english equivalents. He has, however, omitted to include a great many of the less ordinary terms and these lacunae seriously impair its usefulness, especially to translators. The author asks in his preface that users should inform him of omissions which they may observe, and which he hopes to include in future editions. The value of the dictionary would be further increased if explanations and examples of the use of words listed were given. It would nevertheless prove useful to those who use the dictionary in conjunction with works of reference, or in order to check spelling. The orthography of the english equivalents is that of *The Oxford English Dictionary*. It is hoped to follow up this dictionary with a companion volume of english-spanish medical terms.

V. E. C. M.

Practical Food Inspection. Volume I. Meat Inspection

C. R. A. Martin. Third edition. London, H. K. Lewis & Co. Ltd., 1947. vii + 316 pages; 138 figures. 22 × 14 cm. 18s. [£0.9]

Intending sanitary inspectors will welcome a new edition of "Martin", but it could be read with profit by others, particularly medical officers of health. Medical men will probably find the chapters on such diseases as tuberculosis, which occur in both animals and man, of greatest interest.

The work is eminently practical and a mine of information on how to arrive at a "diagnosis" in doubtful cases, e.g., anthrax. A "judgment" is appended to the description of each disease and is particularly useful in such a condition as hydatid cyst, where the destruction of the carcass is not practised as a routine. As the practical nature of the book is stressed it is rather surprising to find no reference to "lumpy jaw" as a synonym for actinomycosis of the jaw bones, either in the text or in the helpful glossary of terms.

The author has illustrated his work with line drawings, but some of these might be omitted, e.g., fig. 71, Tubercle bacilli. It would increase the value of the book to public-health workers if the various Acts and Memoranda referred to in the text were included in the index, somewhat after the style of Clay's *Sanitary inspector's handbook*.

In conclusion, the author presents what at first sight is a dull subject in an interesting manner.

F. T.

Panchito y el Mosco Anofeles

México. Secretaria de Salubridad y Asistencia, Dirección General de Educación Higiénica. México, Secretaria de Salubridad y Asistencia. Dirección General de Educación Higiénica. 7 pages; 6 illustrations. 19 × 15 cm.

This booklet explains to children in a very simple and pleasant way the dangers of malaria, its symptoms and signs, the advisability of consulting the doctor in the early stages, the measures to be taken to protect oneself against mosquitoes—in short, it gives a broad outline of the disease and the remedy. The illustrations are good, both amusing and convincing. Any propaganda directed to children has a repercussion in home life, especially in that of poor peasants who were themselves unable to attend school in their childhood, and who regard their children as a source of wisdom and hope and wish to give them a better chance of life than they had themselves. This booklet probably aims at such results and is a good example of indirect propaganda.

M. V. L.

The Essentials of Materia Medica, Pharmacology and Therapeutics

R. H. Micks. Fourth edition. London, J. & A. Churchill Ltd., 1947. x + 399 pages. 21 × 14 cm. 18s. [£0.9]

"Micks" is probably the most popular, and certainly the most readable of the smaller books on its subject. The present edition has been extensively revised, and all the more familiar newer preparations that one would expect to find have their place. Yet a proper balance is maintained throughout the work. Penicillin occupies nearly a chapter, for example, but streptomycin is dealt with in a few restrained paragraphs as befits a drug whose proper value is not yet known. Special attention has been directed to anaesthetic drugs, and the section on curare alkaloids is adequate. Thiouracil, and its place in the treatment of hyperthyroidism, forms a useful introduction to the use of this drug. One notes with satisfaction that calciferol is discussed in connexion with lupus.

It is sometimes said of the present work that it does not contain enough or that some drugs are excluded that should be included. This is not the fault of the author. The first words of the title are "The essentials", and opinions are bound to differ as to what should be included under this heading. To quote from the preface: "Two aims have been kept in sight throughout the revision, the exposition of the principles which govern the action of therapeutically important drugs . . ." Therefore it is no use searching the index for information on drugs only used for diagnostic purposes such as iodoxyl or pheniodol, even though these are included in similar books on materia medica.

"Micks" is the best introduction to its subject, though in view of what has already been said, prospective examinees should supplement it by reference to other works for some drugs, for example, urethane, which is so useful in the treatment of myeloid leukaemia, but is not to be found in the present edition. The author might consider the inclusion of benadryl in the index when the book is reprinted, especially as it is well described in the text (pp. 188-189).

F. T.

Gas and Air Analgesia

R. J. Minnitt. Third edition. London, Baillière, Tindall & Cox, 1947. vii + 80 pages; 19 illustrations. 18 × 12 cm. 5s. [£0.25]

This little work deals with a big subject, the alleviation of the pains of women in labour by the gas-air analgesia of which the author was one of the pioneers. The apparatus and its assembly, and the technique of its use in midwifery, are briefly but adequately described. Contraindications, causes of failure, applications to minor surgery, and statistics and legislative developments complete the scope of the book. No reference is made to any possible psychic after-effects such as have been described by Dr. Helene Deutsch in the USA.

F. T.

¡ Salud, Madre Campesina !

Esperanza Peña Monterrubio. México, Imprenta "GAMMA", 1941. 21 pages; illustrations. 28 × 21 cm.

In the rural areas of Mexico, whose population seems to be the audience aimed at by the present author, analphabetism is only one of many minor evils. It has long been recognized by experts on social and health propaganda that in such instances posters and illustrations are the best way to convey ideas of behaviour to men and women unable to understand the written word. The author has grasped very aptly the love of music of the mexican countryfolk and has included in this booklet the music of a local tune to which a not very happy litany of health rules is to be sung. The illustrations are not convincing, there being no action explained in any of them except in perhaps two cases: the lazy drunken youth and the hard-working teetotaller. As for the text, although it is advisedly written in very plain and direct language to suit the level of intelligence ascribed to the intended readers, we fail to see why it should be so ungrammatical in a supposedly educational booklet.

In the text, a mother gives advice to her growing daughter concerning both her sexual life, and the dangers of alcoholism and venereal disease in her future husband, which might mar the happiness of their children. She also suggests ways to alleviate the primitive conditions of life in their mud-built dwellings ("jacalitos")—the sad scarcity of water, the absence of drainage or sanitation, in short, some of the many misfortunes associated with a poverty-striken rural area anywhere in the world.

No official authority seems to have sponsored the publication of this booklet.

M. V. L.

Good Health with Diabetes

Ian Murray & Margaret B. Muir. Edinburgh, E. & S. Livingstone Ltd., 1947. vii + 40 pages. 18 × 12 cm. 2s. [£0.1

The purpose of the authors (Physician and Sister-Dietician, Victoria Infirmary, Glasgow) is to provide in the briefest possible form the essential information required by the diabetic patient. In content, price, and format the booklet is suitable to place in the hands of patients themselves. Alternatively, it can be used by the physician as a framework for verbal guidance. The diets have been adjusted to present-day possibilities, and this is, perhaps, the justification for the production of a new work in a field that has already been fairly well covered.

D. T. Richnell

Epidemia Regional de Malaria en la Cuenca del Lago de Maracaibo, 1942-1943. XII Conferencia Sanitaria Panamericana. No. 23

M. Nieto Caicedo. Caracas, Editorial Grafolit, 1946. xx + 288 pages; illustrations. 24 × 16 cm.

Dr. Nieto Caicedo is attached to the malariological division of the Ministry of Health in Venezuela and in this book gives a very full account of the malaria epidemic of 1942–43 in the Lago de Maracaibo district. The first section of the book describes the population of this district, its geographical and climatic characteristics and the distribution of anopheles throughout the area. Section II gives data relating to the epidemic, which lasted for five months and was preceded by exceptionally heavy rainfall. Statistical tables show the numbers of people affected in different towns and districts. Section III relates the anti-epidemic measures adopted, which included the free distribution of quinine tablets, anopheles control, and press and radio educational propaganda. It is hoped that this book will be of interest and use to malariologists who may be called upon to combat a similar epidemic.

V. E. C. M.

Old people

Nuffield Foundation. Report of a Survey Committee on the Problems of Ageing and the Care of Old People, under the Chairmanship of B. Seebohm Rowntree. London, Geoffrey Cumberlege, Oxford University Press, 1947. vii + 202 pages; illustrations. 21 × 14 cm. 3s. 6d. [£0.175]

Though the problem of extreme and unrelieved poverty in old age has largely been met, there remain many hardships of which the available evidence is too often disjointed and scattered. The work of the Nuffield Committee is therefore highly valuable for its collection and presentation of facts. It included in its survey men over 65 and women over 60. It studied their incomes, their living conditions, the institutions provided for their care, their amusements and their possible capacity for work.

The Committee recognized the hardship of loneliness of old age and the evil consequences for old people, living alone, when mentally or physically they may be unfit to care for themselves. It hoped for a solution of the problem in the provision of special homes which should avoid any suggestion of "institutional" atmosphere. Attention was given also to the potential value of old people's clubs. The Committee further gave considerable attention to employment for the aged, not only as a contribution to national prosperity, but as a means of retarding senility. Its recommendations, based on the survey, deserve the closest attention.

A Medical Sub-Committee reported on schemes of research, either begun or projected, into the process of ageing. It suggested that there should not be any centralization of this work, but that the programme might be co-ordinated by the Medical Sub-Committee or similar body, which would advise on fellowships and grants in support of independent workers or teams of workers attacking special problems.

The report has 15 appendices giving information on present-day provision for the aged, on the conditions of life of certain selected groups and on the form of questions asked by the field-workers in carrying out the survey.

P. W.

A Synopsis of Hygiene. (Jameson and Parkinson)

G. S. Parkinson. Ninth edition. London, J. & A. Churchill Ltd., 1947. viii + 791 pages; 16 illustrations. 22 × 14 cm. £1 8s. [£1.4]

The fact that a book has run through many editions is sufficient evidence that it is meeting a need. This is undoubtedly so with "Jameson and Parkinson", which now reaches its 9th edition, for it has established itself as *the* textbook for students preparing for the Diploma in Public Health. Sir Wilson Jameson and Lt.-Col. Parkinson were for a dozen years in charge of the teaching for this examination at the London School of Hygiene and Tropical Medicine and were thus in the best possible position to know the needs of students. The 1st edition, by Jameson and Marchant, published in 1920, was a slim volume of only 404 pages. In the 2nd (1927) to 6th (1939) editions, by Jameson and Parkinson, it grew steadily to 687 pages, and the further two editions, by Parkinson alone, have brought it up to very nearly twice the size of the 1st. The assistance of Miss Kathleen M. Shaw, which is acknowledged in the prefaces from the 5th edition onwards, now receives full and well-deserved recognition on the title-page.

In this latest edition we miss the section on personal hygiene by Professor G. P. Crowden, which had been a feature of the 4th to 8th editions. Indeed, the subject as such appears to have been dropped from the book altogether and there is no reference to it in the index. About a third of Professor Crowden's chapter, dealing with nutrition, does however now appear in Section IV, though this fact is not mentioned either in the preface or the text. The increase of 72 pages over the previous edition is due to new legislation (Education Act 1944, National Health Service Act 1946, National Insurance Act, 1946); to new topics, such as the insecticide DDT; and to fuller treatment of many topics, e.g., food poisoning, occupational diseases and hygiene, and hospitals. Appendix V, containing the full text of the new rules for the Diploma in Public Health which came into operation on 1 January 1946, is a very handy feature for the student.

References to the literature are not very numerous and statements such as "Gray in 1928 found paratyphoid bacilli in seven out of twenty specimens . . . and Begbie and Gibson in 1930 found the same organism in seven out of fifty-seven specimens . . ." are occasionally made without any reference at all being given. The method of scattering bibliographic citations throughout the text not only distracts the eye of the reader but makes it very difficult to pick out a particular reference when one is consulting the book for this purpose. When, as happens in many cases, a long string of references is given at once, it is not always clear which author belongs to which title, etc. These are minor faults, but attention to them in future editions would ease the task of those who use this book as a work of reference.

Cyril C. Barnard

Blood Pressure and its Disorders Including Angina Pectoris

John Plesch. Second edition. London, Baillière, Tindall & Cox, 1947. xiv + 307 pages; 125 illustrations. 22 × 14 cm. £1 1s. [£1.05]

The author starts out with the most laudable intentions, namely, to restrict "the scope of the book to those matters of which I have personal experience through research and observation", and to refrain "from 'rehashing' what can be found in any standard work". Bearing these statements in mind, and the fact that he was formerly Professor of Internal Medicine in the University of Berlin, it is not surprising to find that the book has many references to foreign literature, and is written in a dogmatic, yet conversational style. New references and case-histories have been added in this edition, and the author is at his best when describing symptoms. Some readers will think that the importance of rest in angina pectoris is insufficiently stressed, and that overmuch space is given to smoking, in what the author admits is an "unconventional discussion." The diet chart of foods "permitted" in angina makes nostalgic reading in these days of worldwide shortages. There are too few monographs on the subject of blood-pressure disorders, and this one should prove a useful addition to the literature of the subject.

F. T.

The Rhesus Factor

G. Fulton Roberts. London, William Heinemann Medical Books Ltd., 1947. vii + 47 pages. 18 × 12 cm. 3s. 6d. [£0.175]

The development of research on blood transfusion, stimulated by the discovery of the rhesus factor in 1939 and by the Second World War, has led to discoveries of prime importance to all concerned with the diagnosis and treatment of haemolytic disease. It is the purpose of this booklet by Dr. Roberts, Medical Officer to the North-East London Blood Supply Depot, to acquaint the clinician with the elements and less controversial aspects of the subject. The social implications both of blood transfusion and of disease due to the Rh factor are such that the layman is bound to recognize their significance for himself. This account, therefore, may well prove of interest to readers other than medical men.

Dr. Roberts states that he has a propaganda purpose: "Since . . . every test . . . employs some serum from a patient who has at some time been immunised . . . it behoves every clinician to co-operate in obtaining such sera. Nearly all patients who have been sensitised are in a condition to spare 100 c.c. or more of their blood before the antibody titre fails." *Verb. sap.*

D. T. Richnell

Zählrohrmethoden im medizinischen Forschungslaboratorium

F. Roeder & R. Reiter. Göttingen, Vandenhoeck & Ruprecht, 1947. 35 pages; 15 illustrations. 21 × 15 cm.

In this booklet of 35 pages the authors intended to set out the elementary principles of the construction and operation of Geiger-Müller counters and of the necessary electronic circuits (amplifiers, quench-circuit, thyratron scaling circuit). It was meant for the use of technicians and assistants in biological and medical laboratories and therefore the emphasis throughout is on practical matters, although the technical details given seem hardly sufficient to enable the uninitiated to construct his

or her own Geiger-counter. There is no mention of the bell-shaped end-window type of counter which is so extensively used both in the USA and in Great Britain, especially in connexion with the biological application of radioactive isotopes. Because of the particular purpose of the booklet one would have liked to be given practical examples of actual radioactive assays also, especially of isotopes with weak energy radiations, and a fuller discussion of problems of sample mounting. The usefulness of this publication seems very limited indeed, compared with some american publications of recent years. Biologists would welcome a concise account of problems of radioactive assay; unfortunately this pamphlet does not fulfil the task of providing sufficient instruction, either practical or theoretical.

G. Popják

Common Skin Diseases

A. C. Roxburgh. Eighth edition. London, H. K. Lewis & Co. Ltd., 1947. xxxi + 497 pages; 213 illustrations; 8 plates. 22 × 14 cm. £1 1s. [£1.05]

The problem of what constitutes a "common" skin disease can never be finally settled, and the author has justifiably added a number of further conditions to his new edition. It has also been brought up to date by the inclusion of recent experiences with sulphonamides, penicillin and DDT in dermatology. Most welcome is the recognition accorded to the promising treatment of lupus vulgaris with calciferol. The chapter on varicose veins, eczema and ulcer has been re-written and new illustrations have been added. Beyond recording these improvements there is no need to commend this invaluable work to the general practitioner. The standard of production is well maintained, and if one wishes for further coloured plates, this is only a tribute to a work that deserves them. The author himself offers his apology for the necessary increase in price.

D. T. Richnell

The Childbearing Years

G. Scott Russell. Oxford, Blackwell Scientific Publications, 1947. vii + 88 pages; 11 figures. 22 × 14 cm. 7s. 6d. [£0.375]

This book was written by the author because he felt that young women need a book about themselves, which they can read and digest at leisure and in the seclusion of the home, and which can help them to live fuller and more interesting lives. It is written primarily for those between the ages of seventeen and thirty, but the author adds that parents, teachers and others may find it both interesting and of value.

There is no doubt that this book is a valuable addition to the literature dealing with various aspects of reproduction. It differs from many of its predecessors in that it gives much more anatomical detail as well as a good deal of information about various abnormalities which may arise during the childbearing years. For this reason it is not suitable to be put into the hands of every young woman between the ages of seventeen and thirty, but should only be given to those who have the educational background to understand what they read, and in particular, who are able to place the knowledge they acquire of abnormality in its true perspective. The same remarks apply to the use of this book by parents and teachers, although to a less extent.

Provided the limitations of its use are thoroughly understood this book can be recommended.

J. M. M.

Cerebro-Spinal Fever. Report by the Infectious Diseases Sub-Committee of the Scientific Advisory Committee, on a Comparison of Penicillin and Sulphonamide Treatment of Meningococcal Meningitis in Young Children

Department of Health for Scotland. Edinburgh, His Majesty's Stationery Office, 1947. 13 pages. 24 × 15 cm. 4d. [£0.0167]

The Scientific Advisory Committee of the Department of Health for Scotland has now produced a second report on the treatment of meningococcal meningitis, supplementary to that published in 1944. It compares the results of penicillin and sulphonamide treatments given alternately, as far as possible to children under 5 years of age. The treatment was carried out in five large hospitals for infectious diseases. The dosage schedule for sulphathiazole (or other active sulphonamide) was similar to that recommended in War Memorandum No. 10 of the Medical Research Council. The penicillin scheme of treatment consisted of 200,000 units systemically on the first day of treatment and 5,000 units intrathecally each day for four days for children under 1 year of age, and double these amounts for children of 1 to 5 years.

The number of cases treated was, unfortunately, too small for statistically significant results to be obtained. Nevertheless, *the results exhibit a clear trend in favour of sulphonamide treatment.* Although this result was converse to the expectation of the authors it was in line with the impression gained clinically as the trial progressed. The actual figures showed 11 unsuccessful results with penicillin out of 35 treatments, compared with 5 unsuccessful results with sulphonamides out of 31 treatments. When the age distribution of the two groups is taken into account, however, the superiority of sulphonamides is even more apparent, for less than half of the penicillin cases, and as many as two-thirds of the sulphonamide cases, were in the unfavourable age group under 1 year. An additional group of 15 cases, which all recovered, received treatment with both drugs, and although no conclusion can be drawn from this the Committee has embarked on a further investigation of the effects of the combined treatment. Certain minor findings of the report are that sex distribution may be neglected in any comparison of results, that the age-group under 1 year should be separated from that of 1 to 5 years, that the occurrence of complications was a most important factor in determining the outcome, and that the duration of illness before admission, that is, delay in starting hospital treatment, appeared to be a factor in worsening prognosis.

The complications which are enumerated appear to indicate that all the cases under treatment were the "ordinary form" of the disease. It is to be hoped that in future enquiries the Committee will be able to include fulminating septicaemia and other highly fatal forms of the disease, for it is in these that the combination of sulphonamides and penicillin is likely to be most successful.

H. S. B

The National Health Service Act, 1946. Being the Complete Text of *The National Health Service Act, 1946*, with an Introductory Explanation of the Act

J. A. Scott. London, Eyre & Spottiswoode Ltd., 1947. 108 pages. 24 × 15 cm. 9s. 6d. [£0.475]

In the heat generated by the controversy over the operation of the Act this book comes as a cooling influence. The text itself is available elsewhere, so its value lies in the amplifications, which consist of an index and an introduction. The index, compiled by the Librarian of the Inner Temple, is an expert piece of work and will enable those desiring ready reference to particular points to secure it without wasted effort.

The contribution of Dr. Scott, Lecturer on Hygiene in St. George's Hospital Medical School, is an introduction which sets out in dispassionate terms the steps which brought the Act into being and analyzes its contents. He devotes several pages to the Draft Interim Report of the Medical Planning Commission of the British Medical Association and to the problem of the health centres. He draws attention to the importance of representation of "consumer" interests on administrative bodies, thus emphasizing that patients as well as doctors must have their say. The introduction is only the first word on a subject on which the last will not be written for a very long time, but it enables the reader to see in perspective the aspirations for a greatly improved and comprehensive health-service which have motivated the Act.

D. T. Richnell

Survey and Field Treatment of Malaria in Mauritius

George Sippe & May Twining. Colony of Mauritius. London, Crown Agents for the Colonies, 1946. v + 76 pages; illustrations. 26 × 16 cm. £1 5s. [£1.25]

Mauritius is an island of 700 square miles[1] and has a population of 400,000, or nearly 600 per square mile. The survey, which was carried out in 1942–43 in response to war-time needs, covers the island in detail. The results show that malaria is hyperendemic in the lowland areas and that figures correspond very closely to those recorded by Ross & Fowler in 1908. Greatest incidence is found below 600 feet[2]; during the summer months; and in Creoles and Hindus, the poorest section of the population. In many villages the splenic index is 100%. The effect of chronic malaria on the splenic rate, parasite-rate, carrier-rate and death-rate is discussed. A clear picture of the relationship of the disease to poverty, malnutrition and macrocytic anaemia emerges. The elimination of mosquito breeding-places is not discussed. "Adequate control" was achieved by atebrin treatment, supplemented by improved nutrition, but whether this can be maintained in peace-time is an unanswered question. The conquest of malaria and the conquest of poverty are clearly shown to be interdependent. The survey is admirably produced, printed on one side of the page, with illuminating charts and photographs.

D. T. Richnell

[1] [1 square mile = 2.59 square km.—ED.]
[2] [1 foot = 30.5 cm.—ED.]

Inter-Allied Conferences on War Medicine, 1942-1945: Convened by the Royal Society of Medicine

Edited by *Henry Letheby Tidy.* London, Staples Press Ltd. 531 pages; illustrations. 22 × 14 cm. £2 10s. [£2.5]

From December 1942 to July 1945, 24 conferences on war medicine were convened by the Royal Society of Medicine at its headquarters in London. The objects of these conferences were "the interchange and communication of medical experiences in the Field and of the practical application of medicine to the needs of warfare, and for the exposition of the general principles of administration and organization of the medical services." These objects were achieved

by inviting speakers from the allied forces with the necessary technical knowledge and practical experience. For obvious reasons these meetings were secret, and this book now releases some of the valuable and interesting papers presented. The first meeting opened with an account of the abyssinian campaign, and the conferences followed the course of the war through Libya, Tunis, Sicily and Italy and then from D-day to the german concentration camps.

An interesting section is devoted to vivid descriptions by officers of personal experiences in special episodes. Among these are stories by one who volunteered to remain behind at Dunkirk to care for the wounded, by a medical officer parachuted into Jugoslavia, by another who was dropped into Arnhem, the story of the arctic convoy, and a dramatic description by Professor Richet of 15 months spent in Buchenwald concentration camp. Special subjects, such as malaria, selection of officers and personnel, infective hepatitis and general problems of examination of wounded also received their fair share of discussion. The final meeting was devoted to a review of progress made in war medicine and surgery since 1939 and of the lessons which had been learned. These conferences were held under the presidency of Major-General Sir Henry Letheby Tidy, Consulting Physician to the British Army who, with Dr. J. M. Browne Kutschbach, is responsible for the editing of this volume.

D. F. A.

Massage and Remedial Exercises in Medical and Surgical Conditions

Noël M. Tidy. Seventh edition. Bristol, John Wright & Sons Ltd., 47. viii + 480 pages; 190 figures. 22 × 14 cm. £1 5s. [£1.25]

This is now established as a standard textbook for senior students and junior teachers of physical therapy. The material contained makes no claim to originality, and the treatments recommended are drawn from many sources, but the synthesis has proved its worth. The 6th edition was published in 1944; the author states that only slight alterations have now been made, but there is a new description of carbachol ionization treatment in Raynaud's disease.

D. T. Richnell

An Introduction to Clinical Perimetry

H. M. Traquair. Fifth edition. London, Henry Kimpton, 1946. xv + 330 pages; 255 illustrations. 25 × 19 cm. £1 16s. [£1.8]

This new edition of a standard work is described as "revised and enlarged", but its length and format appear to be almost identical with those of the previous edition. However, it would be mere carping criticism to raise objection to an excellent production on the score of its not being longer. Suffice it that the high level is maintained.

The work has grown with the years from an essay originally written in 1920, and in this edition it has undergone further revision, including changes in the anatomical terminology to "bring it into line with modern usage." It is wholeheartedly to be recommended to ophthalmologists.

D. T. Richnell

Cirugia

Rafael Urzua. Santiago de Chile, Editorial Tegualda, 1947. 691 pages; 100 illustrations. 23 × 15 cm.

This book is based on lectures delivered by the author to his students in the University of Chile. It is intended for students and young surgeons, especially men who are starting a career in surgery in remote districts where they cannot obtain advice from more experienced colleagues in emergencies, or consult works in specialist libraries. The author points out, however, that the art of surgery cannot be learnt from books, but only supplemented by hem.

Professor Uruza, in his section of general observations, offers much useful advice about the surgeon's attitude to his patients, the physical and mental qualities which he should possess or endeavour to cultivate, and pre-operational preparation. The book is simply written and the various operations are clearly described and illustrated. An appendix gives an alphabetical list of words used in surgical terminology, together with an explanation of their meaning in non-technical language.

V. E. C. M.

Modern Treatment Year Book 1947: A Year Book of Diagnosis and Treatment for the General Practitioner

Edited by *Cecil Wakeley.* London, The Medical Press, 1947. viii + 354 pages; 38 figures. 22 × 14 cm. 15s. [£0.75]

This yearbook, now in its 12th year, has firmly established itself on the bookshelf of the general practitioner as a readable and practical textbook of modern diagnosis and treatment. Under the editorship of Sir Cecil Wakeley, 47 specialists have contributed chapters on a wide range of subjects, including influenza, prematurity, pneumonia, various ophthalmic disorders, hysteria and skin diseases. There is an adequate index.

D. F. A.

Practical Biology for Medical and Intermediate Students

C. J. Wallis. Second edition. London, William Heinemann Medical Books Ltd., 1947. ix + 396 pages; 211 figures. 22 × 14 cm. £1 1s. [£1.05]

The 1st edition of this book appeared in 1935 and the 2nd has been revised and reset. It covers the syllabi in biology for the First Examinations for Medical Degrees and those of similar content and is intended as a laboratory manual. It is divided into four sections: Microscopical Technique, Elementary Biochemistry, Plant Biology, and Animal Biology, with appendices dealing with the preparation of reagents, biological methods, etc. There is also a list of firms supplying biological apparatus and material.

L.-J.

Practical Pharmacognosy

T. E. Wallis. Fifth edition. London, J. & A. Churchill Ltd., 1948. ix + 230 pages; 73 figures. 22 × 14 cm. 15s. [£0.75]

This work, now in its 5th edition, is supplementary to the author's *Textbook of pharmacognosy* (Churchill, 1946). It describes the practical investigation into the origins and characteristics of crude drugs as well as the means of identification and establishment of criteria of purity.

The first part of the book deals with the practical study of drugs in common usage and consists of a number of schedules of instructions detailing the observations of greatest importance. Short notes with illustrative sketches are included as well as a certain amount of microscopic work, more particularly of those drugs such as starches, hairs, fibres and broken leaves whose characteristics can be studied only by this means. Guidance in the description of drugs is given, skeleton-reports for the description of plant-members, etc., being included.

The latter and more-advanced half of the book deals with histological and microscopical work. The section on quantitative analysis has been extended by exercises on nux vomica, cinnamon and lycopodium. The use of ultra-violet light is given under the schedule for rhubarb on page 83. The characters of pollen grains as aids to the identification of drugs have been conveniently summarized in a Table and several figures. The histological schedules now include information on the double staining and mounting of botanical sections.

Dr. Wallis is to be congratulated upon this new edition of his manual of practical pharmacognosy. Clearly written, accurately and critically illustrated, it is the standard guide to students reading for qualifications or degrees in pharmacy.

A. Lothian

A Handbook on Diseases of Children: including Dietetics & the Common Fevers

Bruce Williamson. Fifth edition. Edinburgh, E. & S. Livingstone Ltd., 1947. xii + 408 pages; 87 illustrations. 19 × 12 cm. 15s. [£0.75]

The present edition is well produced like its predecessors; the illustrations are an outstanding feature of the book, which is printed on glossy paper of excellent quality. The book is eminently readable, and is constantly enlivened by reference to the author's own experience. Many readers overseas will find the dosages translated in terms of the metric system one of the most useful features of the work. As stated in the preface, the volume "has been thoroughly revised and incorporates treatment by penicillin and other newer compounds." Thus benadryl is mentioned in connexion with angio-neurotic and urticarial conditions.

Rare conditions are mentioned if the author considers them to be important, e.g., chronic constrictive pericarditis, on pages 75–76. The formulary which concludes the book is a most useful feature, though on page 380 only the oral route for the sulphonamides is suggested, and the author does not mention alternative routes if the patient vomits or is unable to swallow. It is true that the intravenous route is indicated in the table on page 381 which is compiled from the Medical Research Council's War Memorandum No. 10 (1943). In the discussion of warts (page 215), no mention is made of plantar warts. But in a work covering such a wide field many readers are bound to regret some omissions, so that such criticisms do not detract from the usefulness of a splendid little book.

F. T.

Biologists in Search of Material: an Interim Report on the Work of the Pioneer Health Centre, Peckham

Edited by *G. Scott Williamson & I. H. Pearse.* Second edition. London, Faber and Faber Ltd., 1947. 107 pages; 5 illustrations. 21 × 14 cm. 5s. [£0.25]

This edition has little new to add to that of 1938 for the very good reason that the war gravely interrupted the work of the Centre, but the present day, with its increasing interest in the problem of national health, is an appropriate time for the appearance of a 2nd edition.

The Peckham Centre is not planned solely for regular medical overhaul and general health guidance. It is not an end in itself but a means to an end—the provision of material for a comparative study of the physical processes of health and wellbeing. That is

does not follow the usually accepted pattern of a health- or community-centre is no valid criticism. In spite of considerable pre-war interest, there remained in many minds much vagueness or misconception about the main object of the Peckham Centre. It is good that this object and the methods proposed for its attainment should be set out again for the sake of the stimulus and suggestions of methods which others may find in a study of the Peckham experiment.

P. W.

Health Services in England

R. C. Wofinden. Bristol, John Wright & Sons Ltd., 1947. x + 191 pages. 19 × 13 cm. 10s. [£0.5]

Awarded the Joseph Rogers prize in 1946 for "the best or only good essay on the treatment of the sick poor of this country and the preservation of the health of the poor", this lucid little book summarizes measures taken in Great Britain to provide for the treatment of the sick and to preserve the health of all social classes. It reviews the achievements of the health services and concludes with a postscript on the National Health Service Act, 1946, placed on the statute book after the completion of the essay.

H. C.

A Text-Book of Gynaecology: for Students and Practitioners

James Young. Seventh edition. London, Adam & Charles Black, 1947. xi + 471 pages; 277 illustrations. 22 × 14 cm. £1 10s. [£1.5]

New editions of this textbook for students and practitioners by the London University Professor of Obstetrics and Gynaecology have been appearing regularly since 1921. The 7th contains many additions and revisions, particularly in that ever-developing sphere, sex endocrinology. The section on ovarian tumours has also been expanded. For all its length the book is conveniently compact, being printed on thin paper, on which the illustrations none the less show up well.

D. T. Richnell

Books Received

October 1947—February 1948

Reviews of many of these books appear in this number of the Bulletin or will appear in future numbers

Abbott Laboratories International Co. *Revision de los conocimientos actuales sobre la penicilina.* 1946. Abbott Laboratories International Co. (Chicago)

Adams, H. S. *Milk and food sanitation practice.* 1947. The Commonwealth Fund (New York); Geoffrey Cumberlege, Oxford University Press (London), 18s. [£0.9]

Alexander, H. L. *Synopsis of allergy.* 2nd ed. 1947. Kimpton (London), £1

Allison, D. R. & Gordon, R. G. *Psychotherapy: its uses and limitations.* 1948. Geoffrey Cumberlege, Oxford University Press (London), 8s. 6d. [£0.425]

Angove, H. S. *Remedial exercises for certain diseases of the heart and lungs.* 2nd ed. 1948. Faber & Faber (London), 10s. 6d. [£0.525]

Arias Vallejo, E. *Disfunciones motoras del estómago.* 1947. Graficas Valera (Madrid)

Bacharach, A. L. *Science and nutrition.* 3rd ed. 1947. Watts (London), 6s. [£0.3]

Bamford, F. *Poisons: their isolation and identification.* 2nd ed., revised by C. P. Stewart. 1947. Churchill (London), £1 1s. [£1.05]

Barber, H. *The occasion fleeting.* 1947. Lewis (London), 15s. [£0.75]

Bartley, S. H. *Vision: a study of its basis.* 1941. D. Van Nostrand Co. (New York), £1 1s. [£1.05]

Beaumont, G. E. *Medicine: essentials for practitioners and students.* 5th ed. 1948. Churchill (London), £1 10s. [£1.5]

Beaumont, G. E. & Palmer, K. N. V. *Practical points in penicillin treatment.* 2nd ed. 1947. Churchill (London), 1s. 6d. [£0.075]

Board of Control. *Lunacy and mental deficiency. The thirty-third annual report of the Board of Control for the year 1946. Part I.* 1947. His Majesty's Stationery Office (London), 9d. [£0.0375]

Boyd, W. *A text-book of pathology: an introduction to medicine.* 5th ed. 1947. Kimpton (London), £2 8s. [£2.4]

Breen, G. E. *Essentials of fevers.* 2nd ed. 1948. Livingstone (Edinburgh), 15s. [£0.75]

British Commonwealth Scientific Conference, 1946. *Specialist conference on culture collections of micro-organisms. London, August, 1947. Report of proceedings.* 1947. His Majesty's Stationery Office (London), 6d. [£0.025]

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Films

The four films reviewed in this section have been completed by Imperial Chemical Industries Ltd. and are designed as visual aids to medical instruction. They were shown at the XVII International Physiological Congress in Oxford in July 1947, *and are important in that they mark the return to the front rank, after a lapse of some years, of films dealing with physiology and physiological techniques*

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Perfusion of the Living Animal [Dog]

made at Department of Physiology, Edinburgh University; owned by Imperial Chemical Industries Ltd.; technical adviser, Professor I. de Burgh Daly; directed by Cyril Jenkins; unit, Film Producers' Guild; available in 16 mm. sound, 1,600 feet [488 m.]; kodachrome; 34 minutes

For a number of years Professor I. de Burgh Daly and his colleagues in the Department of Physiology at the University of Edinburgh have been engaged in the study of pulmonary vasomotor and bronchomotor activity. The perfusion apparatus which they designed for the unequivocal proof of pulmonary vasomotor activity is demonstrated in this film. It is substantially the same as that described by Daly *et al.* in 1942 (*Quart. J. exp. Physiol.* **31**, 227), but with some added refinements; the need for such an elaborate apparatus is well explained in this paper.

In order to ensure that recorded changes in pulmonary arterial pressure were due solely to pulmonary vasomotor nerve stimulation, certain desiderata were also postulated in the same paper. These included a constant systemic arterial pressure; constant inflow of blood to the lungs; constant pressure in both auricles; negative pressure ventilation of the lungs; maintenance of the functional integrity of the pulmonary nerves; separation of bronchomotor from vasomotor effects on pulmonary pressure. It was also desirable that the animal should remain alive during the experiment; that it should not suffer from anoxia at any stage; that the state of the blood should approach normal; and lastly that the depth of anaesthesia should be under exact control all the time.

The film starts with a general view of the whole apparatus and is followed by one of a model which is rotated so that the essential parts can be seen from all sides. Next follows a diagram of the perfusion circuit which is in two parts, systemic and pulmonary.

Heparinized and filtered blood from several donor dogs flows from the first reservoir to the "systemic" Dale-Schuster pump which replaces the left ventricle. From this pump the blood goes to cannulae in the femoral arteries, thence via the systemic circulation of the whole animal to reach the right auricle. From the right auricular appendix a cannula and tube lead the blood to a second reservoir. The pulmonary circulation is from this reservoir to a second Dale-Schuster pump which passes it by means of a specially shaped cannula through the right ventricle into the pulmonary artery and thus to the lungs. The blood returning to the left auricle is led by a cannula and tube back to the first reservoir, thus completing the circuit. The auricles continue to beat throughout the experiment as their blood supply is intact. In addition to the perfusion circuit already described there is a Hooker-Drinker oxygenator shunted across the reservoirs. In this shunt the blood is exposed to a gas mixture of 95 % O_2 and 5 % CO_2 which keeps it oxygenated and maintains the pH at 7.2. With this system the respiratory centre may remain active for about eight hours.

The operating table is electrically heated and the reservoirs and Dale-Schuster pumps are immersed in a thermostatically controlled water-bath. For the preliminary stages positive pressure ventilation of the lungs is needed and is supplied by a Starling "Ideal" pump. Later, when negative pressure ventilation, which more nearly approaches normal respiration, is required, a metal chamber is slid over the operating table and fixed in an airtight manner. The chamber is connected to a vacuum pump providing continuous suction. Respiration is controlled by the admission of air to the chamber by a mechanically operated valve.

The tracheal cannula is connected to a closed respiration circuit which includes a soda-lime absorber for CO_2, a respirometer giving a kymograph record, and provision for the admission of oxygen and for cyclopropane. This anaesthetic is used during the experimental, as opposed to the preliminary operative, period.

The film then shows the various stages of the operation in considerable detail and with great clearness. The dog is anaesthetized, usually with chloralose, and its trachea is exposed, cannulated, and connected to the respiration pump. Great care is taken to secure haemostasis, use being made of diathermic

electrocoagulation for the purpose. The cervical vagosympathetic nerves are exposed and picked up on loose ligatures for stimulation at a later stage.

The heart is exposed and ample time allowed for the firm clotting of any small oozing vessels. This is important, as heparin is given later. The phrenic nerves are crushed to prevent diaphragmatic movements from interfering with tracing recording respiration. The pericardium is opened and the heart supported in a special cradle.

The blood from the donor dogs is equilibrated with the gas mixture; the reservoirs are filled and the pumps started, their outflow cannulae temporarily discharging back into the reservoirs. The femoral arteries are exposed and heparin is given intravenously. A manometer-recording on the kymograph is then connected to a cannula in the left common carotid artery so as to obtain a record of the systemic blood pressure. The femoral artery cannulae are then inserted, though their attached tubes are temporarily clamped and the "systemic" pump turned off.

Special cannulae are inserted into the right and left auricular appendices, connected, as already described, to the reservoirs. The systemic side of the perfusion is now begun by opening the clamps on the tubes leading to the femoral cannulae and starting the systemic pump.

The final stage of the operation is the insertion of a long curved cannula into the pulmonary artery, which is done by making an incision in the tip of the right ventricle and passing the cannula through the heart. It is held in place by strong tapes tied firmly round the whole heart and embracing both ventricles. The pulmonary pump is started and adjusted to give a pressure of 25 mm. Hg which is also recorded on the kymograph.

The operation is now complete and some experiments can be done while the lungs are still working with positive pressure respiration. For example, the addition of 5 μg. of adrenalin to the right auricular reservoir causes a temporary rise in blood pressure. The increase in frequency of the auricular beats is beautifully demonstrated in the film by a close-up view of them. Increasing the output of the systemic pump leads to a rise in systemic blood-pressure as shown on the kymograph record. Conversely, stopping this pump causes the pressure to fall and there is a period of apnoea which results as well. The effect of square-wave stimulation of the thoracic nerves is also shown in the film.

The sliding metal chamber is then put in place and the effects of negative pressure ventilation are demonstrated. Observation of the animal is still possible through a glass lid.

The pressure in the pulmonary artery falls owing to a diminution in the resistance of the pulmonary vascular bed. Vagal stimulation, after eserine, leads to bronchoconstriction and a fall in blood pressure due to stimulation of vasodilator fibres. Adrenalin, 5 μg., injected into the tube leading to the pulmonary artery, causes a rise in pressure in that vessel. Adrenalin after ergotoxin leads to pulmonary vasodilation as shown by a fall in pulmonary arterial pressure; there is later a fall in the systemic blood pressure.

From this summary it can be seen that the experiments demonstrated are particularly well suited to reveal the presence of the pulmonary vasomotor fibres. The technique will, however, undoubtedly be of considerable value in the elucidation of other problems in the physiology of the cardiovascular and respiratory systems.

The film is beautifully produced and the spoken commentary is a model of lucid expression. It should serve as an example of all that a film, designed to demonstrate both an operative technique and physiological phenomena, should be.

A. G. Sanders

1286 (with 1287)

The Humoral Transmission of Sympathetic Impulses

made at Department of Pharmacology, Oxford University, 1947 ; owned by Imperial Chemical Industries Ltd. ; technical adviser, Professor J. H. Burn ; directed by Cyril Jenkins ; unit, Film Producers' Guild ; distributed by Imperial Chemical Industries Ltd. ; available only in 16 mm. sound, 700 feet [213 m.] ; kodachrome ; 14 minutes

1287

The Properties of Acetylcholine

made at Department of Pharmacology, Oxford University, 1947 ; owned by Imperial Chemical Industries Ltd. ; technical adviser, Professor J. H. Burn ; directed by Cyril Jenkins ; unit, Film Producers' Guild ; distributed by Imperial Chemical Industries Ltd. ; available only in 16 mm. sound, 700 feet [213 m.] ; kodachrome ; 22 minutes

The first of these films records an experiment designed to show that the contraction of smooth muscle induced by stimulation of its nerve-supply is effected not by an electrical phenomenon, but by the local release of a chemical substance at the nerve-endings. The argument which the experiment is designed to prove is first shown by diagram : the nerve-supply to a smooth muscle is stimulated ; if then a chemical substance is released it should be detectable by the contraction produced in a distant smooth muscle whose nerve-supply has been interrupted.

The superior cervical ganglion in a cat is removed on one side, and an injection of adrenalin given. The response of the nictitating membranes, to which lever-and-pulley recorders have been attached, is seen on the kymograph: the operated side shows a greater response, thus exhibiting an increased sensitivity over the normal. Next the splanchnic nerves are divided and stimulated: this produces a negligible response on the normal side, but a marked response on the operated side greater even than that produced by the dose of adrenalin. Now the suprarenals are isolated and removed; when the splanchnics are again stimulated the affected side contracts significantly, while at the same time the blood-pressure tracing rises; the normal side shows no response. So it is shown that stimulation of the splanchnic nerve must have released from the gut some such substance as is produced by the adrenal glands.

The pictorial quality and the smooth exposition of this film combine to present clearly and memorably the argument intended. It is, by its subject-content, a specialized film of use only for physiology students, but here it should find routine use in the standard curricula, for it is short enough to be fitted into the normal lecture—indeed, it presents the subject more forcefully and in a shorter time than has been possible hitherto.

* * *

The second film—on the properties of acetylcholine—starts with a portrait of Sir Henry Dale, then presents the chemical structure of acetylcholine and next discusses the one-time mystery —why administration of this drug in small doses produces a fall in blood-pressure, but in large doses a rise. Sir Henry Dale's classical investigations are then repeated. In a cat-preparation a small quantity of the drug injected produces a fall in blood-pressure; by repeating the experiment on an isolated limb it can be seen that this fall must be due to arteriolar dilation. A larger dose of the drug produces a sharper fall in blood-pressure, due to superadded inhibition of the heart; this effect soon passes off, but the blood-pressure remains depressed to some extent, due to continuing arteriolar dilation. A similar effect on the heart can be produced by stimulation of the vagus, while the effect of acetylcholine on the isolated heart mimics vagal stimulations in the intact preparation. Atropine is an antagonist to acetylcholine. The raising of blood-pressure by high doses of acetylcholine is explained by its stimulant action on the suprarenals. Electrical stimulation of the superior cervical ganglion produces responses in the eye which are exactly repeated when the ganglion is painted with acetylcholine.

Here then we have a number of classical experiments collected in some semblance of order, and clearly presented for students to see. Perhaps there are rather too many items for the film to be used in one continuous length as made here; the lecturer may prefer to use it part by part, or else to discuss the whole subject-content fully before putting on the film as a conclusive summary.

* * *

It is interesting to note that these two films, together with the highly specialized "Perfusion of the Living Animal," represent the first physiology films to have been made for a number of years. Physiologists were for many years in the vanguard of film teaching, but during the last decade they have shown a tendency to cede this position to others. These three films put them once more to the fore; they are clear, and free of trimmings, admirably

conceived and executed, and commendably succinct. Not too fast for the audience they are designed for, they resist the temptation to consider side-issues or to loiter over non-essentials. The colour quality is excellent, the commentary (in English) clear, and the kinematic direction scientific and polished. Full use is made of close-up; and kymograph tracings, so often the stumbling-block to smooth pedagogy in these physiological films, are presented clearly and interestingly and are supplemented to the full by the commentary.

1288

The Physiology of the Kidney

made at University College, London ; owned by Imperial Chemical Industries Ltd. ; technical advisers, Professor F. R. Winton & Dr. J. Richardson ; directed by Cyril Jenkins ; unit, Film Producers' Guild ; available in 16 mm. sound, 2,000 feet [608 m.] ; kodachrome ; 45 minutes

This film demonstrates the relationship between renal function and the state of the circulation. It is suitable for medical students, and for revision purposes.

The film begins by showing the gross anatomy of the organ. A model shows the interrelation of the renal blood-vessels and the nephrons at a series of different magnifications. That the formation of urine from the blood takes place in the glomeruli by a process of ultra-filtration is illustrated by several experiments. The preparation used throughout the film is that of a dog anaesthetized with pentobarbitone (nembutal). In the first experiment an intravenous injection of half-strength egg albumin is given. Egg albumin has a molecular weight of 34,000, which is about half that of the plasma albumin. Urine samples are collected before and after the injection and tested for protein. The thick, white precipitate that is formed in the specimens collected after the albumin has been administered proves that this substance is freely excreted by the kidney. The animal next receives an injection of Evans blue, a dye of very high molecular weight, which does not colour the urine, whereas, when phenol red is given, the urine rapidly becomes pink, owing to the excretion of the dye. Phenol red, of course, has a very much smaller molecule than Evans blue. These in vivo experiments are followed by one in which the two dyes are put into cellophan tubes and immersed in water. Phenol red diffuses through the cellophan, whereas the Evans blue does not. Collectively, these experiments indicate that the urine issuing from the glomerulus is an ultra-filtrate of the plasma.

The preparation of the animal and the kymograph records are then explained in greater detail. Arterial pressure is recorded by a cannula in the femoral artery, venous pressure by one in the external jugular vein; the urine outflow of the right kidney and the pressure in the left ureter are recorded also. The effects on the excretion of urine of variations in the circulation are next demonstrated. A rise in systemic blood pressure does not cause an increase in the flow of urine, because the renal vascular system compensates for the rise in pressure. The intravenous injection of adrenalin also causes a rise of blood pressure and a slowing of the heart beat. The renal arterioles, however, are also constricted so that the flow of urine stops instead of being increased. The absence of any direct control over the renal blood vessels by the vagus is shown.

Electrical stimulation of the vagus causes a fall in arterial blood pressure which in turn lowers the pressure in the glomerular capillaries and results in a decrease in the output of urine. Stronger stimuli of the vagus cause at first a rise of venous pressure as well as a drop in the arterial pressure and again the output of urine is diminished. After the period of stimulation there is one of over-compensation when these effects are reversed.

The effect of a sudden and severe haemorrhage is next shown. Very little change occurs until about 180 cm.^{3} of blood have been withdrawn, corresponding to a loss of about 2 litres in a man. After this amount has been withdrawn, the compensatory mechanism fails and there is a fall of arterial pressure with a slight drop also in the venous pressure. The result on the kidney is a diminution in the flow of urine. Restoration of the blood volume by the intravenous infusion of 200 cm.^{3} of physiological saline restores the arterial pressure and also the glomerular filtration pressure. The flow of urine returns to normal and even rises above normal because the dilution of the blood with saline inhibits the re-absorption of water from the urine as it passes through the renal tubules. Normally in man this re-absorption is very considerable.

Diuretics act in two principal ways, either by an increase in the glomerular filtration rate or by causing a decrease in tubular re-absorption of water. The mode of action of caffeine and of two of the "osmotic" group of diuretics is demonstrated in detail.

The film finishes with a résumé of the effects shown, illustrated by the complete kymograph record.

A. G. Sanders

1289

Catalogue of Medical Films

compiled by The Royal Society of Medicine and The Scientific Film Association. London, Aslib, 1948. vii + 125 pages. 19 x 15 cm. 7s. 6d. [£0.375] (6s. to members of Aslib and SFA)

Part I. Title list of 800 films viewed. (i) Alphabetical cross-reference; (ii) subject-group index; (iii) numerical cross-reference. Part II. Details of 200 films arranged in numerical order. Appendix: the Scientific Film Association; the Royal Society of Medicine; Aslib.

This is a well-planned and comprehensive catalogue which will be invaluable to the growing number of users of medical films. An increasing amount of interest is being shown in the possibilities of the film as an aid to medical education and the appearance of this catalogue is therefore most welcome. Its compilation was made possible as a result of collaboration between the Royal Society of Medicine and the Medical Committee of the Scientific Film Association, although, since 1946, the Scientific Film Association has continued the work alone.

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